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Pharmaceutical compounds in waters. Investigations on hospital effluents as a source of environmental contamination and on their treatability

Settore Scientifico Disciplinare ICAR/03

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Abbreviations

AC : Activated carbon

CAS : Conventional Activated Sludge

CBZ : Carbamazepine

CW : Constructed wetland

DW : Drinking Water

EDC : Endocrine Disruptor Compounds

FC : Fecal coliforms

GW : Ground Water

H-SSF : Horizontal Subsurface Flow

HRT : Hydraulic Retention Time

HTM : Hazardous and Toxic Materials

HWW : Hospital Wastewater

i.e. : Inhabitant equivalent

IWW : Industrial Wastewater

MBR : Membrane Biological Reactor

MDR : Multiple drug resistant (bacteria)

MF : Microfiltration

PAA : Peracetic acid

PBT : persistence, bioaccumulation, and toxicity

PEC : predicted environmental concentration

PhC : Pharmaceutical Compound

PNEQ : predicted no-effect concentration

PPCP : Pharmaceutical and Personal Care Product

RQ : risk quotient

SBR : Sequencing Biological Reactor

TC : Total coliforms

THM : trihalomethane

UF : Ultrafiltration

UWW : Urban Wastewater

WW : Wastewater

WWTP : Wastewater Treatment Plant

CHAPTER 1

Introduction

The activity research done during this Ph.D., was born as an overview of pharmaceutical compounds (PhCs) in wastewaters (WWs). In particular, the aim of this work was evaluate the occurrence of these emerging pollutants in the hospital's wastewaters (HWWs), considered one of the main sources of these contaminants in the public sewage and in the environment. To do this, many water samples (withdrawn from different kind of waters: groundwaters, surface waters, drinking waters, urban wastewaters, hospital wastewaters, bottle waters) were analyzed in order to investigate the problem and have more data to compare HWWs with urban ones. The chemical's analysis includes conventional macropollutants like BOD_5, COD, SS, N compounds... as well as pharmaceuticals (till 73 compounds were monitored).

Currently, in Italy and in many other countries, HWWs are assimilated to urban effluents: they are discharged into public sewage, where they are mixed with urban wastewaters (UWWs) and then, they are conveyed to the municipal wastewater treatment plant (WWTP), where they are co-treated.

This practice is acceptable when the effluents of a small hospital discharge in a large WWTP. In this case the *dilution* from the UWWs decreases the pollution load.

But if a large hospital discharges in a small WWTP and so HWWs represent a high percentage of the total water treated, this could represent a problem. In this

new case is important to guarantee an adequate treatment to remove all the macro and micro pollutants that characterize HWWs.

The aim of this thesis was also to focus the attention on the appropriate treatment in function of the effluent's kind, the flow rate and the environmental final conditions. This is because, in general, existing WWTP was built to remove mainly conventional pollutants, like carbon or nitrogen fraction, and not specifically for PhCs.

In Italy the only required pretreatment for HWWs is a mild chlorination, with the objective of decrease of the bacteriological load. This came from a sanitary aspect. In fact, in the first part of last century, there was supposed that these WWs were really dangerous from a bacteriological point of view. Currently, in HWWs, the concentration of bacteria and viruses (excluded infectious diseases department that requires a specific account) are in the same order of magnitude of the urban ones. For this reason, a chlorination of a raw WW (with all the problems facing in this practice, it can cause during the formation of secondary compounds substances like trihalomethane THM and other) is a useless practice if the hospital effluent have to be discharged in a public sewage or co-treated in a biological WWTP.

On the basis of our studies, the local sanitary authority stopped the chlorination of raw HWWs to the health structures of Ferrara's Province. All the Emilia-Romagna Region is discussing about this, in order to stop this expensive and environmental dangerous practice.

1.1. Topic and aims

An important aspect of this thesis is about the building of the new Ferrara's Hospital. It is a structure designed for 900 beds, 5 km far from the town. At this moment the hospital of Ferrara is located in the center of the town, and the WWs deriving from this structure are mixed with the UWWs and discharged in the Ferrara WWTP, designed for 130 000 inhabitants equivalents (i.e.) for the urban line and for 100 000 i.e. for the industrial line (see figure 1.1 for more details).

It is easy to understand that, at present configuration, the town hospital is not a relevant problem, because it represents only a small percentage of the total WWs conveyed to the WWTP and it is correct to consider the Ferrara WWTP a plant

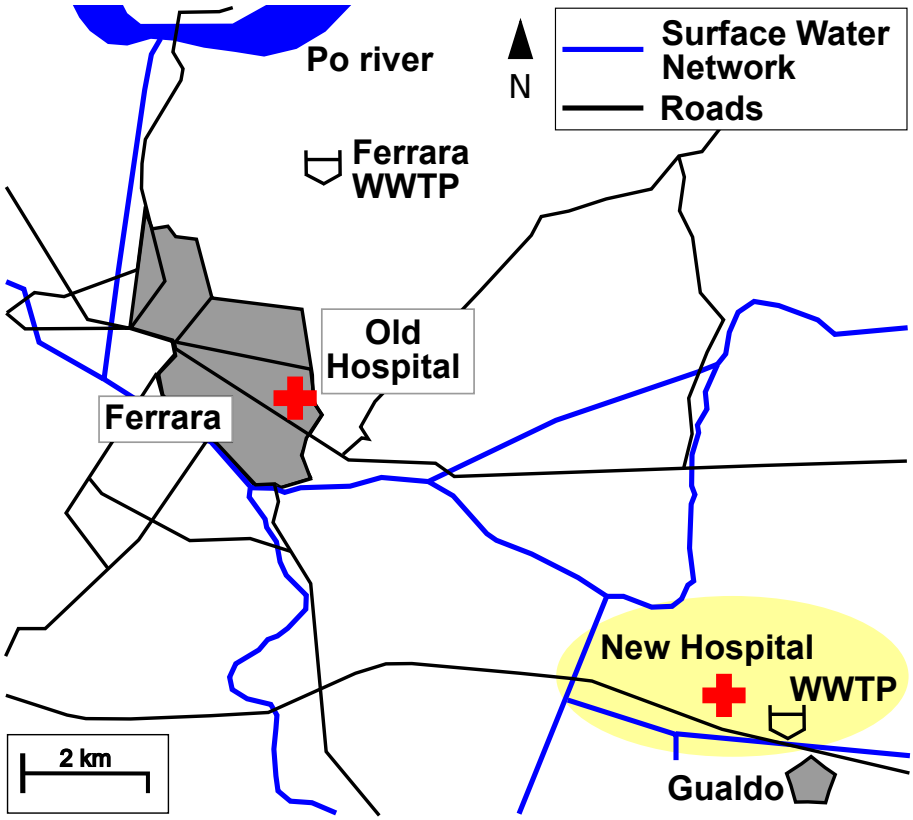


Figure 1.1.: Map of the Ferrara zone with the old and new hospital under construction

treating only UWWs.

But, in the configuration of the new hospital, the WWTP will work with a mixed WWs deriving from a small town, and the contribution of the hospital will increase in a variable percentage: from 16% to 70%.

In this circumstance it is correct to consider the WWTP a dedicated plant for the hospital. For this reason it is important to adopt all the possible technologies to limit the final environmental impact of this particular effluent.

The new Hospital is under construction and, for this reason, the research about the characterization of the HWWs was made in Ferrara Hospital and in another new hospital in Lagosanto, 30 km far from Ferrara, with a capacity of 300 beds, that discharge his WWs in a WWTP mixed with UWWs.

For these reasons this thesis does not focus the attention on the new Hospital, it tries instead to create different backgrounds in the managements of its WWs.

1.2. Structure of this thesis

This work is divided into 6 chapters (including this introduction and the conclusions) and 5 appendixes. To the end of the topic, there is a complete Bibliography with almost 300 citations.

All the chapters are divided, where possible, in two parts: the first one is on the literature aspects of the treated argument, and the second one is on the (original) experimental investigations performed about the specific topic treated in that chapter. In fact, more than 6 experimental investigations were carried out in these years of study.

Chapter 2 explains the diffusion of PhCs into the environment. It starts from a literature's basis that explains the occurrence, fate of PhCs, the health risk and the consequent ecotoxicological effects; the experimental investigation regards different samples taken from surface waters of Po River, groundwaters (GW) from the first aquifer below the Po River and drinking waters (DW) at different steps of the Ferrara's waters work.

The aim of this chapter is investigate the occurrence of PhCs in the environment (by comparing our conclusions to the literature results) and verify if the treatments adopted at water works of Ferrara, could guarantee a sufficient removal of the investigated compounds.

Chapter 3 represents the central chapter (the core chapter) of this work. It refers to hospital and urban effluents, it compares these two kinds of WWs in terms of flow rates and concentration and loads of conventional macroparameters (mainly BOD_5, COD, SS). It also discusses edges and disadvantages of the practice consisting in the direct discharge of the raw hospital effluents in public sewage and subsequent co-treatment.

All these treated aspects are about the basis of literature and they compare them data with the data that we will find in our experimental investigations. The final part of the chapter show the analytical results done on PhCs in two real hospital effluents that have been studied (Lagosanto and Ferrara).

In this chapter are also analysed the different water consumption in the hospital structures because for a single user (the typical user in the hospital is normally the

patient, expressed in terms of bed) the water consumption is really different from the *usual* inhabitant equivalent.

Chapter 4 explains all the experimental investigation carried out in these research years. The chapter is divided in 6 sections.

Each section takes in consideration a different experimental investigation.

The first section regards the raw hospital effluents disinfection. This kind of treatment should not be the only and the first one but in some developing countries, where WWTPs are not presents, hospital's effluents should be at least pre-treated by sedimentation and disinfection before they will be discharged into the environment.

The aim of the research was evaluate the correct dose of disinfectant (peracetic acid or hypochlorite) used for direct discharge of raw effluent into the environment, in order to avoid health and environmental risks.

The second experimental campaign was about the treatment of the raw hospital effluent of Lagosanto (near Ferrara, 300 beds) where two different MBR pilot plants (with equipped microfiltration and ultrafiltration membranes) were tested by analysing macroparameters and some PhCs. This experimental section had the purpose to compare the MBR performance with the CAS, one with respect to macro and micro parameters.

Also the experimental campaign performed in La Spezia WWTP (north west of Italy, see figure 1.2 to see the geografical position) compared the difference between conventional treatments (CAS) and MBR performances, but in this case, the feed to the plant was the UWWs. In the final part of this investigation was also tested a final treatment with ozone.

A further investigation was done at Ferrara's WWTP, in order to evaluate the contribution in the removal of 73 PhCs by a CAS and a polishing treatment, that consist in a horizontal subsurface flow system.

During this investigation in Ferrara's WWTP, two different study steps were developed. The first one using the effluent of the WWTP as influent of the CW, in order to evaluate the final efficiency by removing the 73 studied compounds. The second one add a mixture solution of Ciprofloxacin, Sulphametoxazole and Trimethoprin at the influent of the natural system, with the aim of verify the efficiency of the natural treatment with high concentration of the spiked compounds.

Figure 1.2.: Italy map with Ferrara and La Spezia geographical position

The final section of this chapter discusses and compares the different tested technologies, with particular attention to the natural systems and to the concept of the multibarrier system able to remove a great number of PhCs from WWs.

Chapter 5 is mainly focused about the different technologies that are able to remove the PhCs on the basis of a deeper literature's research. The chapter deals the physico-chemical treatments, the conventional and advanced biological treatments, the nanofiltration technology, the reverse osmosis, the chlorination, a rapid overview about ozonation and AOPs treatment, the natural polishing treatment and, to conclude, the photodegradation.

In the last part, the chapter presents and deals the treatment sequence adopted on the effluent of the new hospital under construction near Ferrara (900 beds), which was also defined on the basis of the experimental investigation carried out at the Department of Engineering of the University of Ferrara to which I took part.

In the final chapter conclusion, recommendation and suggestions are reported.

1.3. Pharmaceutical and Personal Care Products (PPCPs)

Pharmaceutical and Personal Care Products (PPCPs) are a set of chemical pollutants resulting from pharmaceutical and products for personal hygiene. They include a wide and diverse range of chemicals, including prescription drugs and medicines, perfumes, cosmetics, sunscreens, cleansers, shower gel, shampoo, deodorant and other.

Figure 1.3 shown an example of the chemical structure for some PhCs.

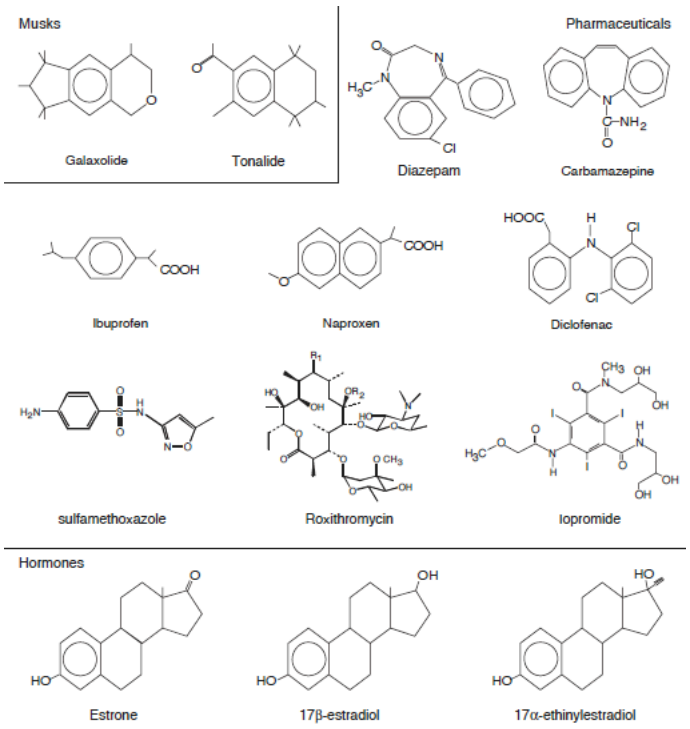


Figure 1.3.: Structure of some PhCs

Many drugs and cosmetic products containing substances and chemicals that are not easily degradable, which remain biologically active, even when they are placed in sewer networks. Among the main causes of the overload of PPCPs include hospitals, nursing homes, veterinary clinics, farms, and not least common housing.

Residues of pharmaceuticals have been found as contaminants in wastewater, surface water, groundwater and drinking water. Residues resulting from use of therapeutic drugs in medical care, are discharged into bodies of surface water, through discharges of different WWTP, which acts as a source of contamination.

Until now, the environmental assessment, for this new class of contaminants, is not yet clear or regulated.

It is reasonable to assume that their presence in waters is not a new phenomenon, it has become in recent decades thanks to the continuous evolution and improvement of methods for chemical analysis that led to a lowering of detection limits for a large number of xenobiotic compounds in environmental matrices.

Identification, analysis, and characterization of the risks posed by the presence of PhCs in the environment, are important issues to concern within the scientific community. Many studies have demonstrated that UWWs are the major pathway for aquatic contamination by pharmaceuticals, since conventional WWTPs are not able to efficiently remove some of these substances, and consequently, they are able to enter surface and drinking waters.

1.4. Regulation

The only Italian legal requirements before the release of this WWs into public sewage is a mild disinfection with sodium ipochloride. In some countries, disinfection was required for the treatment of infectious diseases ward, and then all the hospital effluents were subjected to it. In Italy, Local Sewage Codes quite always require:

- a disinfection step before release into a public sewage,
- a minimum hydraulic retention time in the contact time equal to 30 mins,
- a maximum concentration of active chlorine equal to 0.3 mg L^{-1} in the effluent release into the sewage.

In France, in force law recommends:

- a separated sewage for HWWs,
- a screening for black WWs before release,
- a disinfection for WWs from infectious diseases wards.

Beier et al. (2011) report that in German the Ministry for the environment and the International Association of Waterworks in the Rhine catchment area and its

members (IAWR (2008)) set the value of 100 ng L^{-1} for each micropollutant in case of direct recharge of the aquifer, and also to the recommendation of the German Ministry for the environment. It should be considered that the mentioned target value applies to water systems, which are part of drinking water supplies. In the context of HWWs treatment, this target value is of interest and the treated water is to be directly discharged into waterways, without going through the municipal WWTP.

Moreover, depending on the daily load discharged into the public sewer, there are limits for the hospital effluent for the following:

- macropollutants: SS, BOD_5, COD, total N, Total P,
- micropollutants: phenol, chromium (VI), copper and its compounds, chromium and its compounds, lead, nickel, zinc, manganese, tin, iron, aluminium, adsorbable organic alogens AOX, total hydrocarbons, fluorine.

Over the last few years, the label *emerging* has been applied to pollutants with such increasing frequency that its meaning is becoming diluted. In reality, those pollutants that are truly *emerging* (those that have just gained entry to the environment - for example, because they are new to commerce) are sometimes confused with those, whose presence has just been elucidated, but which have long been present.

PhCs are not yet included in any priority list either in the US or in Europe. Yet US EPA has made some progress on the lists of potential new DW contaminants by considering herbicide degradates, e.g. atrazine-desethyl, alachlor ESA and other acetanilide degradation products Richardson and Ternes (2005).

Daughton (2004) reports that as the power of analytical chemistry increases, the types of chemicals that can be detected increase, and the limits of concentration at which they can be measured are continually lowered; analytical chemistry plays a key role in expanding and refining our ever-changing perspective of water purity. These chemicals comprise the broad spectrum of anthropogenic chemicals (those purposefully synthesized and indirectly produced by human activities - drinking water disinfection byproducts are one example) as well as *natural products* (those created both by natural physicochemical or biological processes an example being geosmin, the off-flavor bicyclic alcohol produced by certain algae and fungi).

Anthropogenic pollutants gain entry to surface and GWs as a result of manufacturing emissions, waste disposal (e.g., incineration, landfills), accidental releases (e.g., spills), purposeful introduction (e.g., pesticides, groundwater recharge, sewage sludge application to land), and consumer activity (which includes both the excretion and purposeful disposal of a wide range of naturally occurring and anthropogenic chemicals such as PPCPs). All of these sources but the last has long been recognized as major potential routes of pollutant release. Consumer activities have only recently been recognized as a potentially major, long-standing source of uncontrolled nonpoint, disperse pollution.

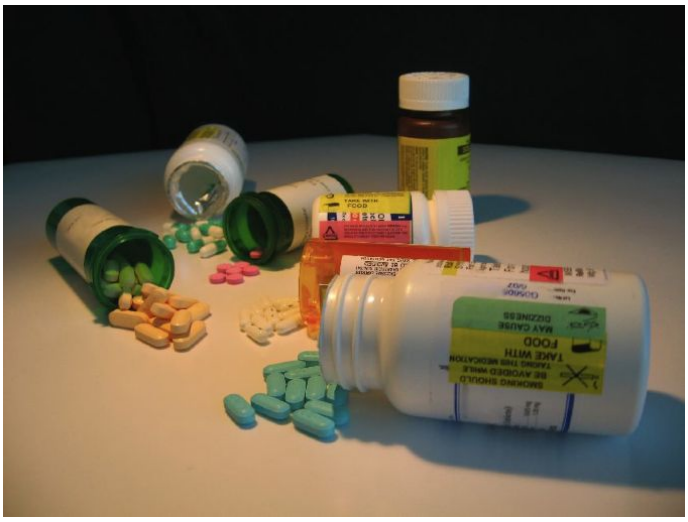


Figure 1.4.: Some PhCs compounds

To get an idea to understand the numbers of distinct organic chemical entities that could hypothetically be synthesized and added to a limitless, ever-expanding known chemical universe, we consider the back-of-the-envelope calculations of Bohacek et al. (1996), which yielded over 10^{60} distinct structures are possible with a total of merely 30 atoms of just C, N, O, or S! Far more than 10^{60} structures would be possible if the wide spectrum of other heteroatoms (including common ones such as P or the halogens) was included, or even larger numbers of C, N, O, and S. Clearly, there are essentially no limits to the types of possible organic chemicals. The possibilities are only beginning to emerge from the efforts of synthetic organic chemists or combinatorial chemistry.

Fuerhacker (2008) explains that there is an increasing threat to human health from exposure to new forms of invisible, time-delayed and more systemic pollu-

tion and chemicals. Especially effects such as cancerogenic, mutagenic and toxic to reproduction (CMR), endocrine disrupting effects or neuro-toxicity are not yet considered in adequate way trough assessment methods and regulatory standards and the application of abatement technologies.

Within Europe, progress in dealing with environmental pressures has been evident in several areas; including substantial reductions in point source emissions to water through the application of abatement technologies and through resource substitution. Nevertheless, to meet the goals of recreational, bathing water and drinking water use, the directives would need to be harmonized with the Water Frame Directive (WFD) also consider microbiological substances.

Despite an explosion of published studies on occurrence, fate, and effects, emerging contaminants discharges to surface waters, are not yet covered by WWTP regulations. Especially, where water is scarce and reuse of WWs is high, treatment of European Commission needs sufficient attention.

Fuerhacker (2008) concludes that, to answer the question if the WFD (2000/60/EC) could reach the target, it provides a very valuable frame to approach the targets, but there is some way to go to reach them on the EU level.

Also in Fuerhacker (2009) these arguments are treated explained that new and existing substances threaten human health and the environment by new forms of invisible and time which are not yet considered in an adequate way through assessment methods and regulatory standards and the application of abatement technologies.

One appropriate tool is REACH (Registration, Evaluation, and Authorisation of Chemicals), which helps to control the sources. Nevertheless, to meet the goals of recreational, bathing water and drinking water use, but also that of WFD and the Stockholm Convention (UNEP 2008, Stockholm Convention. Available at `http://chm.pops.int/`) need to be harmonised and a continuous flexible revision process should react on new developments after appropriate assessment of the hazard or the risk and best available technologies (BAT) need to be developed for the application in the Urban Wastewater Treatment Directive (UWWTD).

In substance watching the European recent legislation and the international agreements there are still some gaps and also the PhCs are among excluded.

Voogt et al. (2009) propose a list of 10 hight priority compounds that was extracted from the literature review work. These compounds represent the minimum that should be considered in any study on pharmaceuticals in water management. This list is only based on compounds already monitored in the literature. This list include:

1. Carbamazepin
2. Sulfamethoxazole
3. Diclofenac
4. Ibuprofen
5. Naproxen
6. Bezafibrate
7. Atenolol
8. Ciprofloxacin
9. Erythromycin
10. Gemfibrozil

CHAPTER 2

PPCPs in the environment

This chapter, as each other, is divided in two main parts, from the section 2.1 to the section 2.4. It describes the presence and the risks of the Pharmaceuticals and personal care products (PPCPs) into the environment. To do this a lot of literature data are reported in order to understand the problem and the diffusion of these compounds.

The second part (section 2.5 and 2.6) will present the experimental investigation results done in different water samples. In particular the analysed waters in these sections were: surface water derived from Po river, Groundwaters (GWs) derived from different wells and from 3 sampling point at different depth level, drinking waters (DWs) derived from different step of the Ferrara's water works.

The aim of this general analysis is compare the diffusion of PPCPs into the environment (mainly surface waters and GWs) and also to discuss about the efficiency of the drinking water treatment in Ferrara.

2.1. Background

The acronym PPCPs was coined in a review article by Daughton and Ternes (1999). Its original intent was merely to serve as a shortcut to refer to Pharmaceuticals and personal care products. The term was subsequently assimilated into the en-

vironmental science literature, presumably for convenience. This broad collection of substances includes any products consumed by individuals or domestic animals for any number of countless reasons pertinent to health, performance, cognitive and phisical function, or appearance (Petrovic and Barcelo (2007)).

The occurrence of Pharmaceuticals compounds (PhCs) in the aquatic environment serves as a timely reminder that not only those substances traditionally target, or those that occur on priority lists for monitoring programs, contaminate the aquatic environment. PhCs are used by man in quantity similar to those of many pesticides. It is therefore hardly surprising that once the analytical instrumentation was established to accurately and specifically analyze for pharmaceuticals in complex environmental matrices they have been detected.

Some of first reports on the presence of pharmaceuticals compounds in the environment were published in 1977 in Hignite and Azarnoff (1977) and 1985 in Richardson and Bowron (1985), whereas the first systematic study on their occurrence in WWTPs and rivers was conducted in Germany from Ternes (1998).

However, research efforts have to be focused on the organic pollutants with the highest hazardous impact rather than on a blanket monitoring. There have been several attempts to prioritize PhACs as environmental contaminants. In the United States (US) Kolpin et al. (2002) selected 95 organic wastewater contaminants (OWCs) among which human and veterinary PhACs, based on their wastewater entry routes into the environment, usage quantities, human or environmental health implications, indication of certain contamination sources or classes of compounds, and availability of analytical methods.

The limited quantity of unpolluted water available for future use as a resource for DW production, is one of the major challenges faced around the world, including Europe. For instance in Mediterranean countries, limited water resources and therefore water quality, is an important economic factor. Indirect reuse can increase the water supply in areas in which the growth of urbanized population has exceeded the quantity of available natural water sources (Ternes and Joss (2006)).

Currently, many communities in Europe and world - wide, use water resources for drinking water production that contain a significant portion of wastewater. So far, strategies for municipal WW treatment have hardly been focused on the elimination

of organic trace pollutants, although for instance prescription and non - prescription *pharmaceuticals and personal care products* (PPCPs) are produced and used by humans in quantities that exceed thousands of metric tons annually.

Approximately 3000 different pharmaceuticals ingredients are used in the EU today, including painkillers, antibiotics, β-blockers, contraceptives, lipid regulators, antidepressants, antineoplastics, tranquilizers, impotence drugs and cytostatic agents.

As these compounds are frequently transformed in the body, a combination of unchanged pharmaceuticals and metabolites are excreted by humans. Human - use pharmaceuticals enter raw sewage via urine and feces and by improper disposal. These pharmaceuticals are discharged from private households and from hospitals and eventually reach municipal wastewater treatment plants (WWTPs). If PPCPs are only partially eliminated, residual quantities enter ambient waters or groundwater. However, direct inputs into natural waters are also possible through storm water overflow and leaks in the sewer system.

Personal care products include the ingredients of shampoos, liquid bath admixtures, skin care products, dental care products, soaps, sun screen agents, hair styling products etc., which are used in enormous quantities throughout the world. In the early 1990s their annual production exceeded 550 000 t for Germany alone (Daughton and Ternes (1999)). Fragrances such as nitro and polycyclic musks as well as UV blockers (e.g. methylbenzyliden camphor) and preservatives (e.g. parabens and isothiazolin derivatives) are also included Ternes et al. (2003). In contrast to pharmaceuticals, personal care products do not have to pass through the human body. They enter the WWs via their regular use during showering or bathing. Frequently they are used as components of cosmetics which mainly consist of lipids or oils (e.g. sun creams) so that a higher lipophilicity is crucial for them.

Figure 2.1 shows the different dimension of the main pollutant parameters into the environment.

The precautionary principle with regard to DW supply and WW treatment, however, implies an efficient removal of all potential harmful constituents. PPCPs are frequently polar and persistent organic compounds, and furthermore possess extremely high biological potency (i.e. estrogens). However, these chemicals recently

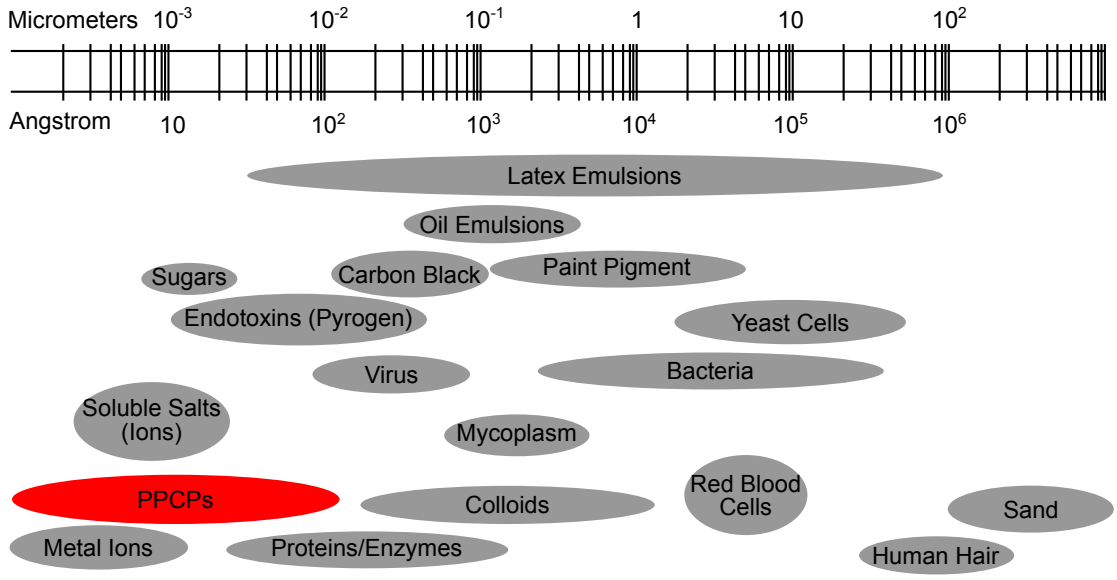


Figure 2.1.: Dimensions of the main pollutant parameters

detected in surface water and drinking water are not considered in the Drinking Water Directive 98/83/EC. The indirect drinking water reuse (unplanned or planned) of municipal WWTP discharges leads to an exposure of the environment and ultimately of drinking water to these chemicals. The removal efficiency of existing wastewater treatment must be optimized and new technologies need to be developed.

PhCs in the environment lately have been acknowledged to constitute a major health risk for humans and members of terrestrial and aquatic ecosystems (Bendz et al. (2005)). Human and veterinary applications are the main sources of PhCs in the environment that are introduced primarily through excretion and the subsequent transport in sewage, whereas direct disposal of unwanted or expired drugs in the sewage is believed to be of minor importance Heberer (2002a).

In the comprehensive reviews (Heberer (2002a), Daughton and Ternes (1999), Halling-Sorensen et al. (1998), Kolpin et al. (2002)), the available data on the occurrence of PhCs in sewage, sludge, sediments, oceans, rivers, and landfill leachate (Holm et al. (1995)) are compiled.

In comparison with conventional priority pollutants, these substances are designed to have specific pharmacological and physiological functions and thus are inherently potent, often with unintended health outcomes in wildlife. Many PhCs do not exhibit an acute aquatic toxicity but have a significant cumulative effect on the

metabolism of nontarget organisms (Halling-Sorensen et al. (1998)) and the ecosystem as a whole Daughton and Ternes (1999). Paramount among these are compounds that interfere with natural hormones, i.e. endocrine disruptors, in nontarget species that act either by design or unintended effect. Many endocrine disruptors induce serious effects in low concentrations (Heberer (2002a), Halling-Sorensen et al. (1998) and Jorgensen and Halling-Sorensen (2000)) but also individual PhCs occurring in low concentrations may exhibit synergistic and cumulative effects. In addition, the development of antibiotic resistance may be stimulated in bacteria from exposure to low concentrations (Jorgensen and Halling-Sorensen (2000)).

2.2. Occurrence and Fate

Profound knowledge of the degradation and fate of PPCPs is important to evaluate the elimination processes in WWTPs and to assess environmental and health risks. Methods should be developed to enable the quantification of PPCPs in wastewater and sludge as well as the partitioning between the aqueous phase and sludge. Furthermore, degradation of PPCPs and information on their metabolites in wastewater and oxidative drinking water treatment are directly related to the efficiency of treatment technologies.

In recent years several studies in Europe and North America were reported which exhibited the occurrence of pharmaceuticals and estrogens in wastewater and ambient waters (Kolpin et al. (2002), Daughton and Ternes (1999), Heberer (2002a)).

In general, the concentrations of PPCPs in WWTP effluents ranged from the ng L^{-1} to the low μg L^{-1} range. In surface waters the concentrations of these compounds ranged mainly between 10-500 ng L^{-1}. Even in ground water and drinking water PPCP residues were detected up to the μg L^{-1} level (Ternes and Joss (2006)). The question arises whether these residues pose risks for aquatic ecosystems or humans.

For this reason in general pharmacologically active compounds that include both legally used pharmaceuticals and illicit drugs, are a group of emerging environmental contaminants, potentially hazardous compounds, that have been receiving steadily growing attention over the last decade Kasprzyk-Hordern (2010).

Surprisingly, there are limited data and minimal understanding of the environmental occurrence, transport, fate and exposure for many pharmaceuticals and their metabolites, despite their frequently high annual usage (Daughton and Ternes (1999), Fent et al. (2006), Carlsson et al. (2006a), Carlsson et al. (2006b)).

Some of the most commonly used pharmaceuticals are sold in the UK in hundreds of tonnes per year. Usage of drugs is going to increase in the future, due to the ageing population in western countries and an increase in consumption levels in the developing world. Illicit drugs, belonging to the same group of biologically active compounds, have however hardly been studied in the environment (Zuccato et al. (2008), Kasprzyk-Hordern et al. (2008)).

Pharmaceuticals and illicit drugs enter the aquatic environment, mainly through treated (or raw) sewage from domestic households and hospitals, waste effluents from manufacturing processes and runoff. Domestic animals are the main direct source of the environmental disposal of many veterinary pharmaceuticals (antibiotics, anaesthetics, etc.), as manure is very often applied to agricultural fields as a fertiliser. Sludge from wastewater plants containing human pharmaceuticals (especially those of more hydrophobic nature) is also used as a fertiliser in agricultural fields or transported to landfill.

Figure 2.2 shows the different concentration of the main pollutant parameters into the environment, from the WWTPs effluents to the natural rivers. The figure includes the macroparameters as BOD_5, COD, SS and microparameters as heavy metals or PPCPs.

A huge percentage of antibiotics such as doxycycline, oxytetracycline and levofloxacin is excreted by the human body unchanged.

The behavior and fate of pharmaceuticals and their metabolites in the aquatic environment is not well known. The low volatility of pharmaceuticals indicates that distribution in the environment will occur primarily through aqueous transport, but also via food chain dispersal. In WW treatment, two elimination processes are generally important: adsorption to suspended solids (sewage sludge) and biodegradation (Fent et al. (2006)).

Adsorption is dependent on both hydrophobic and electrostatic interactions of the pharmaceutical with particulates and microorganisms. Acidic pharmaceutical such

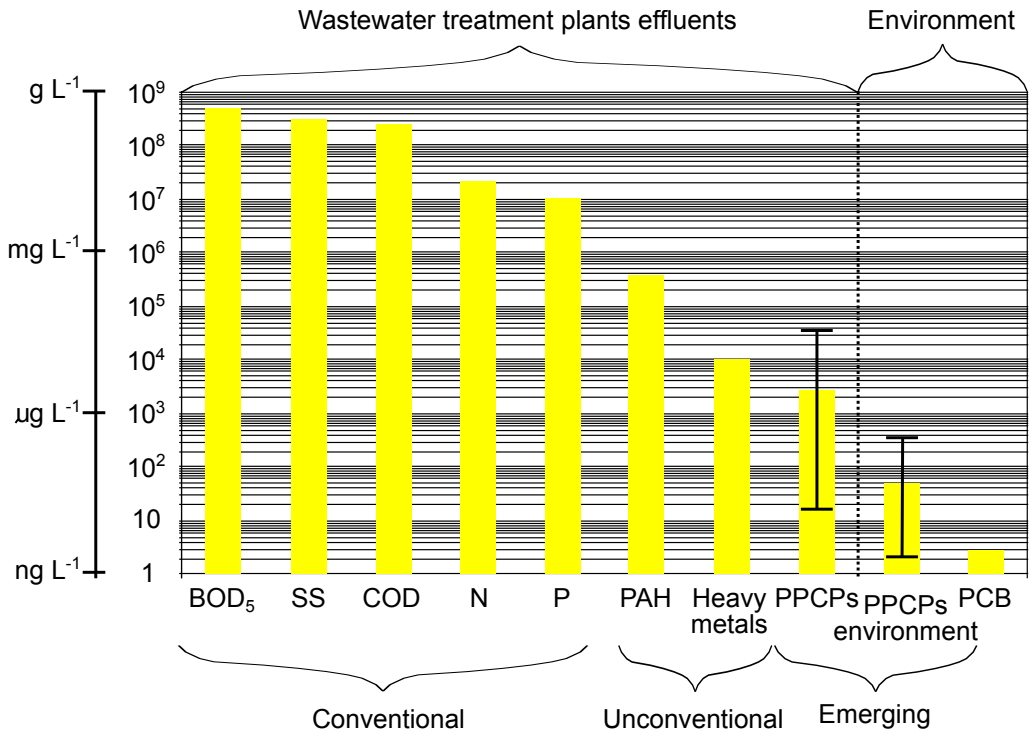


Figure 2.2.: Concentrations of the main pollutant parameters

as the acetylsalicylic acid, ibuprofen, fenoprofen, ketoprofen, naproxen, diclofenac and indomethacin having pK_a values ranging from 4.9 to 4.1, as well as clofibric acid, bezafibrate (pK_a 3.6) and gemfibrozil occur as ion at neutral pH, and have small tendency of adsorption to the sludge. But adsorption increases with lower pH. At neutral pH, these negatively charged pharmaceuticals therefore occur mainly in the dissolved phase in the WW. For these compounds and the antitumor agent ifosfamide sorption by non-specific interactions seems not to be relevant (Kummerer et al. (1997), Buser et al. (1998)). In general, sorption of acidic pharmaceuticals to sludge is suggested to be not very important for the elimination of pharmaceuticals from wastewater and surface water. Therefore, levels of pharmaceuticals in digested sludge and sediments, are suggested to be relatively low, as was demonstrated in several monitoring studies (Ternes et al. (2004a), Urase and Kikuta (2005)). However, basic pharmaceuticals can adsorb to sludge to a significant extent, as has been shown for fluoroquinolone antibiotics (Golet et al. (2002)). For the hydrophobic EE2 ($\log K_{ow} = 4.0$) sorption to sludge is likely to play a role in the removal from WWs (Fent et al. (2006)).

Degradation in sludge seems not significant. As a consequence, EE2 occurs in digested sludge, where concentrations of 17 ng g^{-1} were reported (Ternes et al.

(2002a)). In case a pharmaceutical is occurring mainly in the dissolved phase, biodegradation is suggested to be the most important elimination process in WWTP. It can occur either in aerobic (and anaerobic) zones in activated sludge treatment, or anaerobically in sewage sludge digestion. In general, biological decomposition of micro-pollutants, including pharmaceuticals increases with increase in hydraulic retention time and with age of the sludge in the activated sludge treatment.

For example, diclofenac was shown to be significantly biodegraded only when the sludge retention time was at least 8 days (Kreuzinger et al. (2004)). In contrast, data from Metcalfe et al. (2003a) and Metcalfe et al. (2003b) indicate that the neutral drug carbamazepine, which is hardly biodegradable, is only poorly eliminated (normally less than 10%), independent from hydraulic retention times. Pharmaceuticals are often excreted mainly as nonconjugated and conjugated polar metabolites. Conjugates can, however, be cleaved in sewage treatment plants (STP), resulting in the release of active parent compound as shown for estradiol (Ternes et al. (1999)), and the steroid hormone in the contraceptive pill, 17α-ethinylestradiol (D'Ascenzio et al. (2003)).

Studies on the elimination rates during the STP process, are mainly based on measurements of influent and effluent concentrations in STPs, and they vary, according to the construction and treatment technology, hydraulic retention time, season and performance of the STP. Some studies (Ternes (1998), Carballa et al. (2004)) indicate elimination efficiencies of pharmaceuticals to span a large range (0-99%). The average elimination for specific pharmaceuticals varied from only 7 to 8% for carbamazepine (Ternes (1998), Heberer (2002a), Clara et al. (2004)) up to 81% for acetylsalicylic acid, 96% for propranolol, and 99% for salicylic acid (Ternes (1998), Ternes et al. (1999), Heberer (2002a)).

Lowest average removal rates were found for diclofenac (26%), the removal of bezafibrate was 51%, but varied significantly between STPs, and high removal rates were found for naproxen (81%) (Lindqvist et al. (2005)). Very high total elimination of 94-100% of ibuprofen, naproxen, ketoprofen and diclofenac was found in three STPs in the U.S.A. (Thomas and Foster (2004)). Efficient removal took place mainly in the secondary treatment step (51-99% removal), whereas in the primary treatment only 0-44% were removed. X-ray contrast media (diatrizoate, iopamidol,

iopromide, iomeprol), to the contrary, were not significantly eliminated (Ternes and Hirsch (2000)). This variation in elimination rates is not surprising, since pharmaceuticals form a heterogeneous group consisting of compounds with diverse chemical properties. Independent from the chemical characteristics of the compounds, the efficiencies of various STPs also vary for the same compound due to their equipment and treatment steps but also to other factors such as temperature and weather. For instance, diclofenac showed largely different elimination rates between 17% (Heberer (2002a)) and 69% (Ternes (1998)), and 100% (Thomas and Foster (2004)).

Once in surface waters, biotransformation through biodegradation occurs, but abiotic transformation reactions are probably more important. Whereas hydrolysis is generally negligible for environmentally relevant human drugs, photodegradation sometimes plays an important role at the water surface. Photolysis has been shown to be the main removal process for diclofenac in surface water (Buser et al. (1998)). For additional pharmaceuticals (sulfamethoxazole, ofloxacin and propranolol) laboratory experiments indicate direct and indirect photolysis as an important removal process (Andreozzi et al. (2003)). Carbamazepine and clofibric acid, both compounds that are marginally processed in STP, have been shown to undergo slow photodegradation in salt- and organicfree water with estimated half-lives in the range of 100 days at latitudes of 50 N in winter (Andreozzi et al. (2003)). The efficiency of photodegradation depends, besides substance properties, on the strength of the solar irradiation, and therefore on latitude and season, and on constituents present in the water that may act as photosensitizers generating hydroxyl radicals and singlet oxygen (i.e. nitrates, humic acids). Some adsorption to particles may occur. Laboratory batch studies to characterize the sorption behavior of carbamazepine, diclofenac and ibuprofen in sandy sediments show that sorption coefficients were generally quite low (Scheytt et al. (2005)). Diclofenac and ibuprofen are carboxylic acids with pK_a values of 4.16 and 4.52 and these weak acids are negatively charged at pH of ambient water and sediment.

There is no information about the bioaccumulation potential of pharmaceuticals in biota or food webs with the exception of diclofenac, accumulating in the prey of vultures (Oaks et al. (2004)), fluoxetine, sertraline and the SSRI metabolites norfluoxetine and desmethylsertraline detected in fish. Diclofenac bioconcentration factors

were 10-2700 in the liver of fish and 5-1000 in the kidney, depending on exposure concentrations (Brooks et al. (2005)). A few cases were reported, where pharmaceuticals were detected in drinking water and groundwater (Holm et al. (1995)). Ozonation, granulated activated carbon, and advanced oxidation have been shown as efficient removal processes. In drinking water, this has been shown for diclofenac, while clofibric acid and ibuprofen were oxidized in laboratory experiments mainly by ozone/H_2O_2 (Zwiener and Frimmel (2000)). The elimination of selected compounds (bezafibrate, clofibric acid, carbamazepine, diclofenac) during drinking water treatment, was investigated in laboratory experiments and waterworks (Ternes et al. (2002b)). No significant removal was observed in batch experiments with sand, indicating low sorption properties and persistence. Flocculation using iron(III) chloride was ineffective, but ozonation was in some cases very effective in eliminating these polar pharmaceuticals. However, clofibric acid was stable and not eliminated, even with filtration using granular activated carbon, which was effective for the other compounds. The removal of pharmaceuticals and other polar micro-pollutants, can therefore only be assured, using more advanced techniques such as ozonation, activated carbon or membrane filtration (Ternes et al. (2002b)). However, the economic consequences have to be evaluated carefully, before investing into these advanced treatment technologies on a larger scale.

The drugs that have a low proportion of the parent compound excreted also display a higher concentration in the aquatic environment, suggesting that the low excretion proportions may represent higher recalcitrance in the environment. The data base on PPCP concentrations in the environment is still small, but it is apparent that the concentrations are typically low. Physico - chemical characteristics such as solubility, $\log K_{ow}$, and pK_a are used in pharmacokinetic studies in clinical settings and their use has been transplanted, seemingly wholesale, in predicting the behavior of PPCPs in environmental (Jjemba (2006)).

2.3. Health Risks

The aim of this thesis is not focusing this interesting theme but I think that it is important to speak slowly about this topic.

Lin (2007) defines human health risk, like the probability that a given exposure or a series of exposures may have or will damage the health of individuals exposed.

Risk is the potential for realization of unwanted adverse consequences or events. In general terms, human health risk is the probability of injury, disease, or death under a given chemical or biological exposure or under series of exposures.

Risk may be expressed in quantitative term (zero to one). In many cases, it can only be described as high, low or trivial.

An important concept is that we do not live in a risk-free world, but in a chemical world. There are more than 65 000 chemicals produced, and they are increasing their number every year. Through use and abuse, many of those chemical products will end up in our environment - water, air and land. These chemicals include organics and inorganics that are used in industries (including water treatment plants), pharmaceuticals, agriculture (insecticides), home, personal cosmic purposes, etc.

Escher et al. (2011) report that, despite limitations of the toxicity estimation model, his study gives a comprehensive picture on the risk posed by HWWs. It allows setting priorities for further experimental testing. Interestingly (but disturbingly), the PhCs likely to pose the highest environmental risk, have rarely been investigated previously. No one, or very few experimental data, are available for the physicochemical properties or ecotoxicity of amiodarone, ritonavir, and clotrimazole, the three top-risk compounds in the general hospital. In the psychiatric center, diclofenac was among the three top-risk compounds, together with ritonavir and clotrimazole. Diclofenac is the only one of these pharmaceuticals that is well researched in ecotoxicology and risk assessment.

As this analysis has demonstrated, the predicted no-effect concentration (PNEC) is generally the more important driver for the risk quotient (RQ). The reason is that the variability in the PNEC among all pharmaceuticals investigated is more than seven orders of magnitude, while the predicted environmental concentration (PEC) values cover only three to four orders of magnitude among the group of 100 most used pharmaceuticals. This means that if PhCs are selected only according to their usage pattern and occurrence, one might miss relevant ones that could pose an environmental risk. Therefore, consumption data are less suited to guide prioritization, but often the only available source for compound identification. Thus hazard iden-

tification should precede risk assessment to prioritize according to intrinsic hazard properties such as potential for persistence, bioaccumulation, and toxicity (PBT).

The regulation for industrial chemicals in Europe, REACH, has exactly taken this step by using a PBT assessment to identify chemicals to be prioritized for further testing and risk assessment (EC (2006)). Following this recommendation, the European Medicines Agency's guideline also advises to include PBT assessment in the prescreening phase of risk assessment of pharmaceuticals for pharmaceuticals exceeding a log K_{ow} of 4.5 complementing the exposure estimate as trigger for refined risk assessment (EMEA (2006)).

The ecotoxicological risk assessment is a subset of the ecological risk assessment and can, for this reason, be treated according to an approach of the same type. Ecological risk assessment is a process that evaluates the likelihood of one or more stressors (EPA (1992)). This process is based on two major elements: characterization of effects and characterization of exposure, these provide the focus for conducting the three phases of risk assessment: problem formulation, analysis phase and risk characterization phase (EPA (1998)).

2.3.1. Risk management

Risk management is the identification, assessment, and prioritization of risks followed by coordinated and economical application of resources to minimize, monitor, and control the probability and/or impact of unfortunate events or to maximize the realization of opportunities. Risks can come from uncertainty in financial markets, project failures, legal liabilities, credit risk, accidents, natural causes and disasters as well as deliberate attacks from an adversary. Several risk management standards have been developed including the Project Management Institute, the National Institute of Science and Technology, actuarial societies, and ISO standards. Methods, definitions and goals, vary widely according to whether the risk management method, are in the context of project management, security, engineering, industrial processes, financial portfolios, actuarial assessments, or public health and safety. The strategies to manage risk include transferring the risk to another party, avoiding the risk, reducing the negative effect of the risk, and accepting some or all of the consequences of a particular risk. Certain aspects of many risk is management

standards have come under criticism for having no measurable improvement on risk even though the confidence in estimates and decisions increase.

In other words, it is the process of deciding what to do about the problems.

2.3.2. Risk assessment

Risk assessment is a step in a risk management procedure. Risk assessment is the determination of quantitative or qualitative value of risk related to a concrete situation and a recognized threat (also called hazard). Quantitative risk assessment requires calculations of two components of risk: R, the magnitude of the potential loss L, and the probability p, that the loss will occur.

In other words, risk assessment is a quantitative evaluation process of health or environmental risks determining the potential risks, associated with exposure to a type of human hazard-physical, chemical or biological.

2.3.3. Environmental risk of PPCPs

Wells et al. (2009) shown an interesting review about all the different reports of water quality research and management pertaining to emerging pollutants, either chemical or biological, for which discussion of occurrence surveys, fate investigations, treatment methodologies, modeling, and/or toxicity/risk assessment appearing in the peer-reviewed literature during 2008, are presented.

As reported Eriksson et al. (2008) published a literature review, demonstrating that 541 xenobiotic organic compounds (XOCs) potentially could be present in sewage sludge, due to their presence in construction materials: pharmaceuticals, personal care products, etc.; 192 compounds have been quantified in sewage sludge, which indicated that, although many XOCs have been measured in sludge, there are potentially a vast number of compounds present that have not been analyzed to date. In a hazard identification of the quantified compounds, using their inherent properties and environmental fate, it was shown that 99 XOCs could be classified as being hazardous with regard to the solid phase and 23 were found to be priority pollutants in the subsequent hazard assessment.

Cooper et al. (2008) provided information on pharmaceutical threats to the environment. A preliminary risk assessment database for common pharmaceuticals,

was created and put into a web-accessible database named *Pharmaceuticals in the Environment, Information for Assessing Risk* (PEIAR) to help others evaluate potential risks of pharmaceutical contaminants in the environment. Information from PEIAR was used to prioritize compounds that may threaten the environment, with a focus on marine and estuarine environments.

Fawell (2008) provided a commentary on determining the health risks of microconstituents. He highlighted the inappropriateness of currently accepted risk assessment methods. The author also suggested that an emerging method, the threshold of toxicological concern (TTC) be considered as an alternate method for dealing with prioritization of problems associated with low level contaminants in the diet. In addition, the importance of understanding how to deal with complex mixtures and evaluating catchment control options as part of a holistic approach to addressing risk priorities. The ecotoxicological hazard potential of pharmaceuticals and their human metabolites and of nanomaterials in the aquatic environment, were reviewed by Farre et al. (2008). This work focused particularly on the metabolites and transformation products of emerging pollutants. Ecotoxicological studies of carbamazepine and diclofenac (frequently detected in the aquatic environment) implied that acute toxic effects are not a concern at environmental concentrations, but their chronic and synergistic effects with other compounds need more study, also because sludge retention time did not influence removal efficiencies of either compound.

Life cycle impact assessment (LCIA) was conducted by Munoz et al. (2008) for 98 frequently detected priority and emerging pollutants. The approach was used to study influent and effluent from a WWTP in Spain. Impact scores for two scenarios-discharging wastewater to the aquatic environment and its use for crop irrigation-were evaluated. The data indicated substantial reduction in ecotoxicity and human toxicity, following treatment (42 to 85%). The pollutants causing the greatest share of the impacts were prioritized. Ciprofloxacin, fluoxetine, and nicotine were the primary PPCPs of concern while 2,3,7,8-TCDD, nickel, and hexachlorobenzene were the priority pollutants of greatest impact.

Occurrence of the antibiotics roxithromycin, trimethoprim, and chloramphenicol were studied in STP effluents and surface waters of the Han River, Korea, by Choi et al. (2008). Concentration and frequency of detection of the antibiotics were

greater in effluent samples and in samples collected during the low-flow season. Acute standard aquatic ecotoxicity tests indicated minimal risks to aquatic systems.

Dussault et al. (2008) examined the toxicity of atorvastin (ATO), carbamazepine (CBZ), 17α- ethinylestradiol (EE2), and triclosan (TCS) toward benthic invertebrate species. The toxicity data were applied in a hazard quotient approach. They concluded that potential risks existed toward benthic invertebrates for TCS and CBZ, however, considering low environmental concentrations, ATO and EE2 posted negligible risk to benthic invertebrates.

Safety threshold values for pharmaceutical compounds are limited and often related to single compound-single organism toxicity studies. Many pharmaceutical compounds have not yet been studied as extensively as others and reliable toxicity data are limited to acute effects only. Cleuvers (2003) studied the toxicity of a number of compounds to Daphnia magna including diclofenac, carbamazepine and propranolol. The EC50 values were found to be 68, 72 and 7.5 mgL^{-1} respectively, which are substantially higher in comparison to the concentrations measured in this study at ng L^{-1} range. Nevertheless, it must be noted that the impact of a mixture of these chemicals could prove more toxic than the individual compounds alone. For example, Flaherty and Dodson (2005) found that pharmaceutical mixtures behaved unpredictably and caused serious side effects such as deformities and increased mortality in D. magna.

Due to low pharmaceutical concentrations found in natural waters, their impact in causing chronic toxicity to aquatic populations close to sewage effluents is of more importance. Recently when studying cytological effects of pharmaceuticals in rainbow trout (Oncorhynchus mykiss) and common carp (Cyprinus carpio), Triebskorn et al. (2007) determined that the lowest observed effect concentrations (LOEC) for carbamazepine and diclofenac were 1 μg L^{-1}. Although the highest pharmaceutical concentration (334 ng L^{-1} of carbamazepine) in the river Ouse is still lower than its LOEC, the safety margin becomes relatively constrained. Furthermore, due to the more significant impacts from mixtures of pollutants and potential persistence of such chemicals, it is prudent that these chemicals should be monitored regularly.

2.4. Ecotoxicological effects

Hospitals are the main sources of PhCs in a concentrated area and, together with households and industries, can be seen as significant urban area hotspots for discharging these contaminants into the sewer network and surface waters, with a potential impact on human health (Kummerer (2001); Pauwels and Verstraete (2006); Weissbrodt et al. (2008)). Many drugs used in hospitals (for instance antibiotics and cytostatic drugs) are designed to show signs of DNA damage toward bacteria or eukaryotic cells, raising concern about the human and ecological hazard of hospital effluents (Giuliani et al. (1996), Hartmann et al. (1999)). The contact of hospital contaminants with aquatic ecosystems leads to a risk directly related to the existence of hazardous substances (mainly disinfectants, excreted pharmaceuticals or their metabolites) which could have potential negative effects on the biological balance of natural environments. This risk is defined as the probability of appearance of toxic effects after an organism's exposure to hazardous substances (Rivière (1998)). The fate of pharmaceuticals in the aquatic environment has been reported in different studies (Kummerer et al. (1997); Halling-Sorensen et al. (1998); Heberer (2002b); Golet et al. (2002); Bendz et al. (2005); Bartels and von Tumpling (2008)), and an ecological risk assessment has been carried out for specific compounds: glutaraldehyde, a dialdehyde usually recommended as the disinfectant of choice for reusable fiber-optic endoscopes (Jolibois et al. (2002)), specific antibiotics (Hartmann et al. (1999); Golet et al. (2002), Kummerer and Henninger (2003)), carmamazepine, ibuprofen, ketoprofen and naproxen (Santos et al. (2007)). However, few studies deal with the total risk resulting from simultaneous exposure to the various pollutants present in hospital effluents.

Emmanuel et al. (2005b) describes a proposal framework for the ecotoxicological risk assessment of hospital wastewaters, and the European Medicine Agency (EMEA (2006)) issued guidelines for the environmental risk assessment of medicinal products for human use according to the directive EC (2003) on risk assessment for new notified substances.

Pharmaceuticals are designed to target specific metabolic and molecular pathways in humans and animals, but they often have important side effects too. When introduced into the environment they may affect the same pathways in animals

having identical or similar target organs, tissues, cells or biomolecules. Certain receptors in lower animals resemble those in humans, others however, are different or lacking, which means that dissimilar modes of actions may occur in lower animals. It is important in this respect to recognize that for many drugs, their specific modes of actions are not well known and often not only one, but many different modes of actions occur. Among other reasons, this makes specific toxicity analysis in lower animals difficult to perform. Despite this, toxicity experiments should be targeted and designed for specific targets of the pharmaceutical even in lower vertebrates and invertebrates, based on the hypothesis of similarity of modes of actions. However, current toxicity testing is not designed in this way, rather general and established test systems and traditional organisms according to guidelines are being used and traditional end points such as mortality are assessed.

The current literature (Jones et al. (2002), Carlsson et al. (2006a), Carlsson et al. (2006b), Emmanuel et al. (2005b)) about ecotoxicological effects of human pharmaceutical deals mainly with the acute toxicity in standardized tests and it is generally focused on aquatic organisms. The influence of environmental parameters such as pH on toxicity has only rarely, or not yet been investigated. Such studies would be important for instance of acidic pharmaceuticals, that may induce different toxicities depending on speciation at different ambient pH. Moreover, effects of drug metabolites have rarely been investigated. Phototransformation products of naproxen, for instance, showed higher toxicities than the parent compound, while genotoxicity was not found (Isidori et al. (2005)). At contaminated sites, aquatic life is exposed over the entire life cycle to these compounds. Chronic effects are less investigated and often even related to relative short-term exposures. However, long-term exposures are needed for an accurate environmental risk assessment (Fent et al. (2006)).

2.5. Experimental investigations on ground, surface and drinking water

Starting from this section the attention is focused on the experimental analysis done during this Ph.D. research. All the samples were analysed with the help of the CSIC of Barcelona with the methods reported in appendix A and in Gros et al. (2009).

In the first phase of the experimental investigation the goal was to verify the diffusion of the different PhCs in the environment. In particular different kind of waters were analysed, in order to completely understand the diffusion into the surface water or into the GWs of these compounds. Moreover another important objective of these investigations was to see the abatement capacity of the drinking step in Ferrara water works.

The different analysed samples were:

- surface waters from Po River
- GWs down and near the Po River. The samples were taken at different depth with specific perforation and from existing wells,
- drinking waters in different section of the Ferrara water works

All the investigated compound are reported in table 2.1. Not all the compounds were found in all the different kinds of waters. In appendix A (from table A.1 to table A.7) are also reported the physico-chemical properties of the 73 investigated PhCs. Moreover in table A.11 and A.12 are reported all the compounds and their optimized QqLIT-MS/MS Parameters by SRM negative and positive ionization mode.

Table 2.1.: Investigated pharmaceutical compounds: CAS number and formula. In parenthesis the number of analyzed compounds

Class	**Compound**	**CAS Number**	**Formula**
Analgesics or	Acetaminophen	103-90-2	C8H9NO2
anti-inflam. (12)	Codeine	76-57-3	C18H21NO3
	Diclofenac	15307-86-5	C14H11Cl2NO2
	Ibuprofen	15687-27-1	C13H18O2
	Indomethacin	53-86-1	C19H16ClNO4
	Ketoprofen	22071-15-4	C16H14O3
	Mefenamic acid	61-68-7	C15H15NO2
	Naproxen	22204-53-1	C14H14O3
	Phenazone	60-80-0	C11H12N2O
	Phenylbutazone	50-33-9	C19H20N2O2
	Propyphenazone	479-92-5	C14H18N2O
	Salicylic acid	69-72-7	C7H6O3

Antibiotics (25)	Azithromycin	83905-01-5	C38H72N2O12
	Chloramphenicol	56-75-7	C11H12Cl2N2O5
	Chlortetracycline	57-62-5	C22H23ClN2O8
	Ciprofloxacin	85721-33-1	C17H18FN3O3
	Clarithromycin	81103-11-9	C38H69NO13
	Danofloxacin	112398-08-0	C19H20FN3O3
	Doxycycline	564-25-0	C22H24N2O8
	Enoxacin	74011-58-8	C15H17FN4O3
	Enrofloxacin	93106-60-6	C19H22FN3O3
	Erithromycin	114-07-08	C37H67NO13
	Josamycin	1684-24-5	C42H69NO15
	Metronidazole	443-48-1	C6H9N3O3
	Nifuroxazide	965-52-6	C12H9N3O5
	Norfloxacin	70458-96-7	C16H18FN3O3
	Ofloxacin	82419-36-1	C18H20FN3O4
	Oxytetracyclin	79-57-2	C22H24N2O9
	Roxithromycin	80214-83-1	C41H76N2O15
	Spiramycin	8025-81-8	C43H74N2O14
	Sulfadiazine	68-35-9	C10H10N4O2S
	Sulfamethazine	57-68-1	C12H14N4O2S
	Sulfamethoxazole	723-46-6	C10H11N3O3S
	Tetracycline	60-54-8	C22H24N2O8
	Tilmicosin	108050-54-0	C46H80N2O13
	Trimethoprim	738-70-5	C14H18N4O3
	Tylosin A	1401-69-0	C46H77NO17
Antidiabetic (1)	Glibenclamide	10238-21-8	C23H28ClN3O5S
Anti-hypertensive (3)	Enalapril	75847-73-3	C20H28N2O5
	Hydro-chlorothiazide	58-93-5	C7H8ClN3O4S2
	Lisinopril	83915-83-7	C21H31N3O5
Barbiturates (3)	Butalbital	77-27-9	C11H16N2O3
	Pentobarbital	76-74-4	C11H18N2O3
	Phenobarbital	50-06-6	C12H12N2O3
Beta-agonists (2)	Clenbuterol	037148-27-9	C12H18Cl2N2O

	Salbutamol	35763-26-9	C13H21NO3
Beta-blockers (9)	Atenolol	29133-68-7	C14H22N2O3
	Betaxolol	63659-18-7	C18H29NO3
	Carazolol	57775-29-8	C18H22N2O2
	Metoprolol	37350-58-6	C15H25NO3
	Nadolol	42200-33-9	C17H27NO4
	Pindolol	13523-86-9	C14H20N2O2
	Propranolol	525-66-6	C16H21NO2
	Sotalol	3930-20-9	C12H20N2O3S
	Timolol	26839-75-8	C13H24N4O3S
Diuretic (1)	Furosemide	54-31-9	C12H11ClN2O5S
Lipid regulators (7)	Atorvastatin	134523-00-5	C33H35FN2O5
	Bezafibrate	41859-67-0	C19H20ClNO4
	Clofibric acid	882-09-7	C10H11O3
	Fenofibrate	49562-28-9	C20H21ClO4
	Gemfibrozil	25812-30-0	C15H2203
	Mevastatin	73573-88-3	C23H34O5
	Pravastatin	81093-37-0	C23H36O7
Psychiatric drugs (5)	Carbamazepine	298-46-4	C15H12N2O
	Diazepam	439-14-5	C16H13ClN2O
	Fluoxetine	54910-89-3	C17H18F3NO
	Lorazepam	846-49-1	C15H10Cl2N2O2
	Paroxetine	61869-08-7	C19H20FNO3
Receptor antagonists (4)	Cimetidine	51481-61-9	C10H16N6S
	Famotidine	76824-35-6	C8H15N7O2S3
	Loratadine	79794-75-5	C22H23ClN2O2
	Ranitidine	66357-35-5	C13H22N4O3S
Antineoplastic (1)	Tamoxifen	10540-29-1	C26H29NO

2.5.1. Po River

Literature data

Greater amounts of data are available for surface waters. The number of PhCs that have been targeted and the number of locations samples are significantly greater. Much of these data are of North America and Europe. For example, of 18 antibiotics targeted in German study of river waters as reported in Hirsch et al. (1999), a degradation product of erythromicin was detected in the highest concentration (maximum 1.7 μg L^{-1}), whilst four other compounds were also detected at lower concentrations. Buser et al. (1999) reports that Ibuprofen has also been detected in several lakes and rivers in Swizzerland at concentrations up to 7.8 ng L^{-1} but he did not report the metabolites. The concentration of ibuprofen in this study were low in comparison to studies in other countries like, for example in Ternes (1998) where concentration of over 2000 ng L^{-1} have been reported.

Dilution effects are an important consideration when measuring the concentration of pharmaceutical compounds in rivers and streams. Lipid regulators, bezafibrate and gemfibrozil, demonstrated at 5 - 10 times dilution in rivers receiving WWTP effluent compared to the effluent discharged (Ternes (1998)). Elsewhere, elevated concentrations of drugs detected in a small tributary receiving a large contribution of effluent were rapidly diluted to near detection limits when they flowed into a large volume river (Metcalfe et al. (2003b)) and most pharmaceuticals were only detected in freshwater sites receiving WWTP effluents. However, in the low flow system of a smaller river, virtually no dilution was shown to occur. The hydrology of the receiving water therefore plays an important role in the dilution of any pharmaceutical substances that may be present and is specific to a given location Petrovic and Barcelo (2007). In addition to ibuprofen, other pharmaceutical metabolites have been detected in receiving waters. Clofibrate was not detected in rivers and streams in a German study whereas its metabolite, clofibric acid was present in the ng L^{-1} range as explained in Ternes (1998). Uptake of pharmaceuticals by aquatic organisms is an important consequence of elevated pharmaceuticals concentrations in receiving waters such as effluent dominated rivers and streams. Fish in US streams have demonstrated uptake of the antidepressant, fluoxetine, norfluoxetine, sertraline and desmethylsertraline (Brooks et al. (2005)).

Experimental data

The analysis about the surface water of the Po River were made on March, 23 (1^{st} sample), 24 (2^{nd} sample) and 25 (3^{th} sample), 2010. The sampling point was just in front of Ferrara water works in order to take out some significant samples from the inlet of this plant.

Particular attention was made to the weather condition because it was important that the samples were taken in dry days in order to decrease the rain dilution.

These instantaneous samples were collected in 1 L plastic bottle, they were immediately filtered with a 0.45 μm membrane and refrigerated at -20 ^{o}C till the transport and the preparation for the HPLC-MS/MS analysis in Barcelona.

Only 27 compounds (from the 73 reported in table 2.1) were detected in Po River surface waters and the analytical results are reported in figure 2.3 and showed in table C.2. A lot of compounds were never detected probably due to they lowest concentration in surface waters or due to the more rapid degradation when they are release into the environment. An important aspect of the PhCs degradation into the environment certainly is represented from natural photo-degradation (see subsection 5.1.9 for more details about this topic).

Then, a lot of searched compounds were not detected. This is a key for the next drinking water step. It is also very important to underline that the detected concentration were very low, in effect the highest measured concentrations were for the antihypertensive Hydrochlorothiazide that in the three analyzed samples was detected with a maximum value of 118 ng L^{-1} (average value of 96 ng L^{-1}). The second highest compound detected in this waters was the β-blockers Sotalol find with a maximum value of 84 ng L^{-1} and with an average of 78 ng L^{-1}.

The average values (calculated independent from the kind of compound) of all the detected compounds, as reported in table C.2, are quite constant in the three samples (29, 28, 29 ng L^{-1}) and are really very low. Moreover the sum concentration vary from 593 ng L^{-1} to 756 ng L^{-1}, so with values always lower than 1 μg L^{-1}.

For this reason it is possible to say that the concentration of PhCs in Po River does not represent an environmental problem. Certainly this is due to the highest dilution of this large River that on march present an average flow rate of 1000-1200 m^3 s^{-1}.

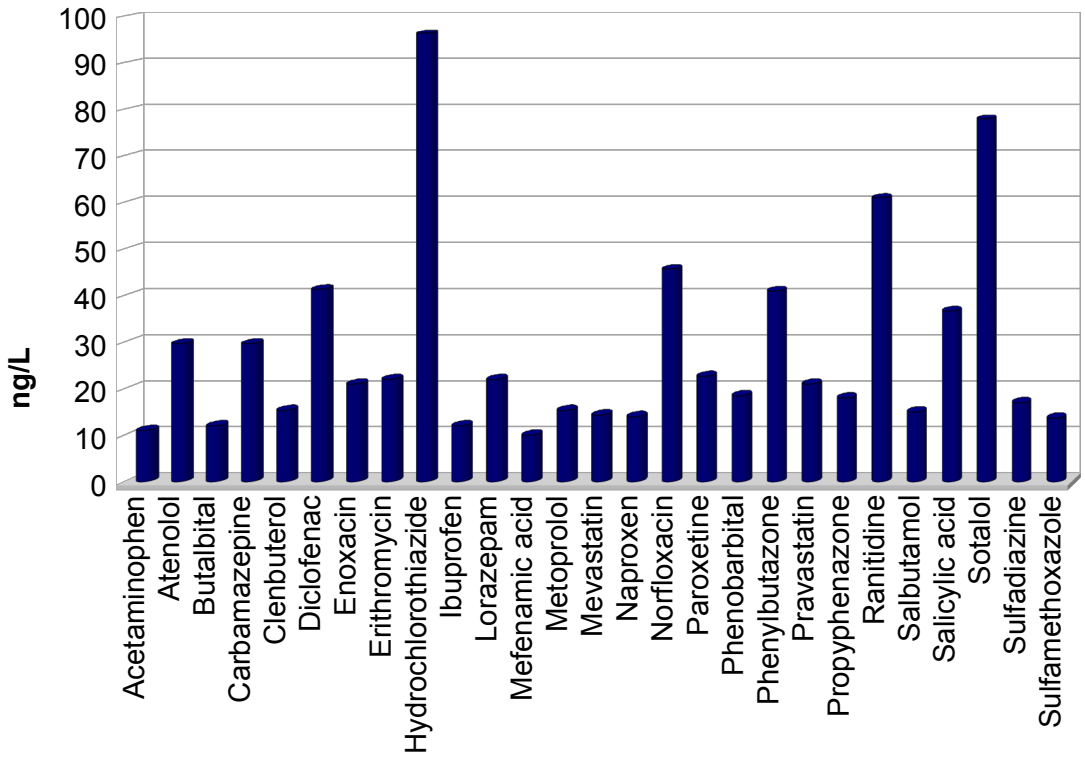


Figure 2.3.: Average values of the analytical results (n=3) of the experimental campaign on Po River waters

2.5.2. Groundwaters

Literature data

Since the mid-1990s there have been reports of the occurrence of PhCs in groundwater. This waters can become contaminated from a number of sources, for example, historic contamination from sites of production, runoff from agricultural land, landfill and wastewater effluent (Heberer (2002a), Heberer et al. (1997), Holm et al. (1995)). The disposal of industrial waste in a landfill site in Denmark has been shown to be the source of PhCs in leachate-contaminated groundwater adjacent to the site (Holm et al. (1995)).

A number of sulphonamide antibiotics (sulphadiazine, sulphamethiozole) were present in groundwater samples collected at concentrations of up to 0.5 μg L^{-1}. The pharmaceutical contamination of groundwater around the city of Berlin in Germany has been extensively investigated (Heberer (2002a), Heberer et al. (1997)). Heberer et al. (1997) and his co-workers have reported the occurrence of clofibric acid, phenazone, propylpenazone, carbamazepine, diclofenac, ibuprofen and fenofi-

brate in Berlin groundwater with wastewater effluent contamination being identified as the source via surface water. In another study conducted in Germany, a number of antibiotics compounds were identified as present in groundwater with application of animal slurry to fields being the likely source due to runoff (Hirsch et al. (1999)).

Sulfamethoxazole was determined at a maximum concentration of 0.47 μg L^{-1} along with sulfamethazine that was detected at a maximum concentration of 0.16 μg L^{-1}. However, these two compounds were only detected in 2 of the 59 samples collected, whilst another 16 targeted antibiotics were below the detection limits of the methods used indicating that the load of antibiotics from livestock treatment to groundwater was small (Petrovic and Barcelo (2007)).

Experimental data

Another goal of this work was the research of the 73 PhCs reported in table 2.1 in GWs. In particular GW derived from three different sampling points at different levels depth were analysed. For major information about the geographical situation and for the sampling depth see figure 2.4 and table 2.2. Figure 2.4 shows the Po river, few km far from Ferrara, the Ferrara WWTP (north-east of the town) and the town water works in the north of the town.

All these samples were taken in september 2009 in the middle of the Po River with a specific perforation instrument, in order to take out water just down the river. In this way all the samples present almost 10 m of natural sand filter.

In these samples, 36 compounds were found and the concentration were variable from ng L^{-1} to μg L^{-1}.

Table 2.2.: Sample date, name and level in GW analytical campaign

Date	**Sample Name**	**Level, m**
September 2, 2009	S1A	18
	S1B	30
September 4, 2009	S2A	18
	S2B	30
September 9, 2009	S3A	9
	S3B	23

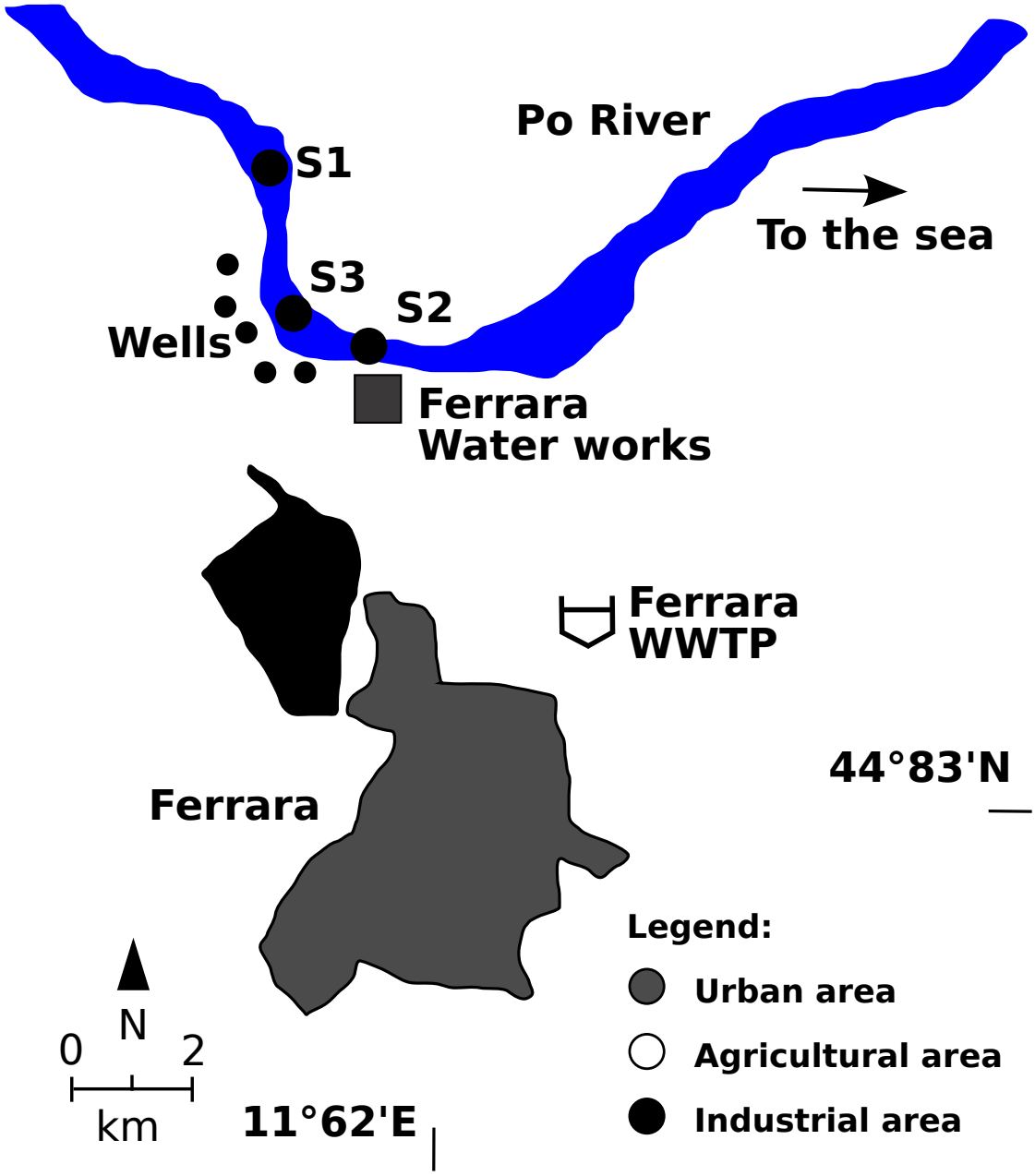


Figure 2.4.: Ferrara scheme with the three sampling point (S1, S2, S3) for the GW analysis

Table 2.3.: GW average and standard deviation in ng L^{-1} with n=6

Compounds	**Average**	**Standard deviation**
Acetaminophen	45	13
Atenolol	67	63
Butalbital	42	–
Carbamazepine	34	–
Chloramphenicol	20	–
Chlortetracycline	26	15
Ciprofloxacin	21	–
Diclofenac	13	–
Doxycycline	133	42
Enoxacin	12	1
Erithromycin	27	20
Fluoxetine	20	8
Indomethacine	739	662
Ketoprofen	475	232
Lorazepam	20	8
Mefenamic acid	99	45
Metoprolol	26	16
Metronidazole	39	21
Mevastatin	204	60
Naproxen	92	53
Nifuroxazide	40	31
Norfloxacin	10	1
Ofloxacin	16	5
Oxytetracycline	45	31
Pentobarbital	27	11
Phenobarbital	32	24
Phenylbutazone	26	18
Pravastatin	31	20
Propyphenazone	13	–
Salicylic acid	36	4

Sotalol	15	–
Sulfadiazine	13	–
Sulfamethazine	71	6
Sulfamethoxazole	11	1
Tetracycline	50	43
Timolol	16	6

Table 2.3 shows the average values and the standard deviation values for the detected compounds in these water sample. For all the analytical results in the different sampling point see table C.3.

Watching the results it is possible to find an accumulation of some substances like for example Indomethacine. Probably this substance find, at 18 m depth, particular aerobic or anaerobic characteristics that cause her accumulation.

Indomethacine is detected at large concentration if compared with the other PhCs. In fact the concentration of this compound vary from 120 ng L^{-1} in S2, at 30 m depth, to 1983 ng L^{-1} in S1, at 18 m.

The hight presence of this and other substances may be due to the punctual and statical sampling extraction. In fact, in order to compare a continuous sampling extraction, water derived from a mixture of wells continuously used to produce drinking waters were analysed. This sample were taken on march 23, 2010 in an instantaneous sample.

Comparing table C.3 with table C.4 it is clear that a continuous sampling of the GWs can improve the water quality due to the fact that there are not point of accumulation.

Paying the attention in the table C.4 and in figure 2.5 it is possible to see tat only 10 compounds were detected and that the concentrations were really slow if compared with those in S1, S2 and S3. In this case the PhCs concentration in wells waters are completely comparable with those in surface waters.

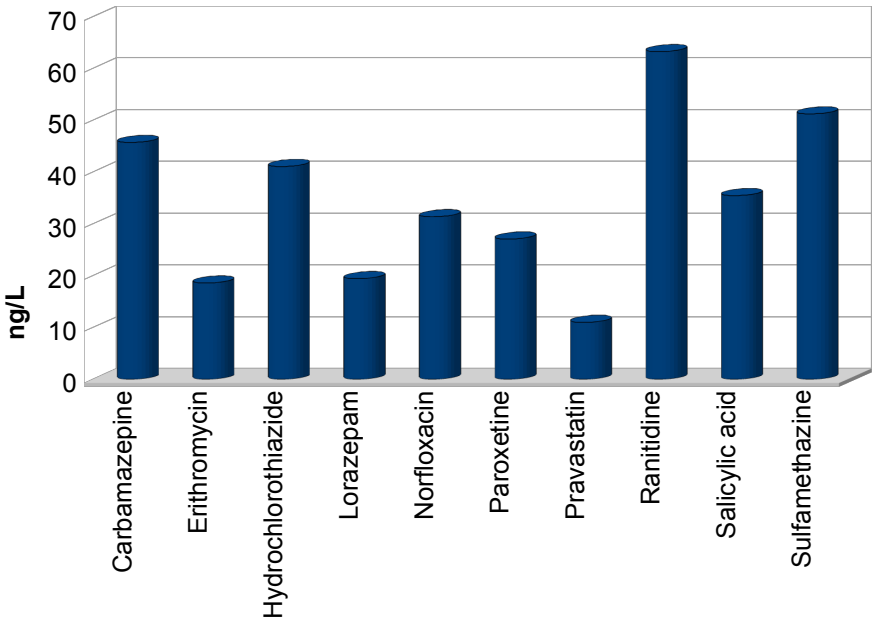


Figure 2.5.: Results of the analysis on the PhCs in the Ferrara wells

2.5.3. Drinking waters

Literature data

In summer 2004, the Observer newspaper in the UK incorrectly reported the alarming news that prozac (fluoxetine) had been detected in UK drinking water (Petrovic and Barcelo (2007)). Alarming as this headline may sound, there have been reports of the occurrence of pharmaceuticals in water intended for human consumption (Table 2.4). Again, occurrence alone may not be a problem since the doses may be well below those required to exert any effect. Potable water treatment is also important since the presence of any contaminant in source water does not mean that it will be present in potable water supplies. It is therefore the effectiveness of any treatment process, if present, that is key to the presence of PhCs in drinking water.

In the early 1990s, clofibric acid, the pharmacologically active metabolite of blood lipid-regulating drugs used in human medical care, was detected in ground- and drinking water samples collected in Berlin, Germany (Heberer and Stan (1997)). This initial discovery was due to the structural similarity between clofibric acid and the herbicide mecoprop. In Berlin, concentrations of up to 165 ng L^{-1} have been reported, whilst concentrations of between 25 and 100 ng L^{-1} have been reported in drinking water collected from The Netherlands (see table 2.4 in wich the data refers

to: Heberer and Stan (1997), Heberer et al. (2002),Stackelberg et al. (2004), Stolker et al. (2004), Reddersen et al. (2002)). Finding clofibric acid in the drinking water of Berlin promted further investigation into the groundwater wells and how PhCs were entering them (Heberer et al. (1997)). Additional work focused on whether other PhCs were occurring in Berlin groundwater and present in drinking water following treatment (Heberer (2002b)). In addition to clofibric acid, carbamazepine, primidone, phenadazone, propylphenadazone and diclofenac have been detected in samples of Berlin drinking water as reported in table 2.4. Elsewhere in Germany, 17-α-ethynylestradiol has been detected at < 1 ng L^{-1} concentrations, whilst also in Berlin, phenazone drugs and their metabolites have been detected in drinking water samples at concentrations of up to 900 ng L^{-1}.

Outside of Germany, carbamazepine has also been detected in drinking water samples collected from the US and the Netherlands. In the US, dehydronifedipine has also been reported to occur in drinking water samples, whilst in the Netherlands the occurrence of acetyl(salicyclic acid), the widely used non-prescription analgesic commonly known as aspirin, and the antibiotic, sulfamethoxazole, have been reported.

Table 2.4.: Examples of PhCs that have been shown to occur in drinking water

Substance	**Highest concentration (ng L^{-1})**	**Location**
Carbamazepine	258	USA
	20	Germany
	< 25	The Netherlands
Dehydronifedipine	4	USA
Clofibric Acid	165	Germany
	25-100	The Netherlands
Primidone	15	Germany
Phenadazone	400	Germany
AMDOPH*	900	Germany
Diclofenac	< 10	Germany
Acetyl(salicyclic acid)	25-100	The Netherlands
Sulfamethoxazole	< 25	The Netherlands

* 1-acetyl-1-methyl-2-dimethyl-oxamoyl-2-phenylhydrazide

Experimental data

The Ferrara water works is located in the north zone of the town and it takes water from the Po River as reported in figure 2.4. It presents a maximum water production capacity of 1.2 m^3 s^{-1}. In general the average load is approximately 0.9 m^3 s^{-1} and the water is taken for the 80% from surface Po River and for the other 20% from different wells near the plant.

The DW is obtained with different step of treatment and the treatment is different for waters derived from Po River and water taken out from the wells.

Figure 2.6 shows the treatment step used in Ferrara water works to produce DW from two different kind of waters.

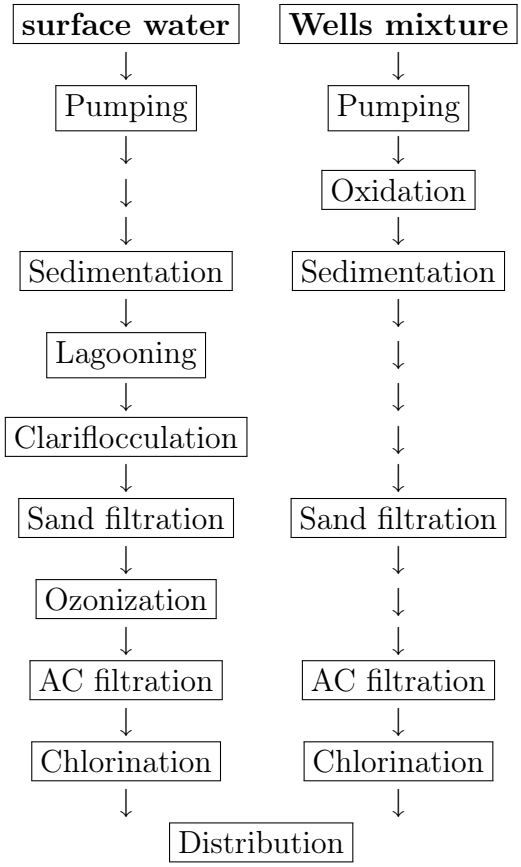


Figure 2.6.: Water works step in Ferrara

In order to understand the abatement capacity of the step used in the Ferrara water works, some samples were taken after lagooning, clariflocculation, ozonization, Activated Carbon (AC) filtration, and chlorination (this samples represent the effective tap water distributed in Ferrara). Only one instantaneous sample was taken for each sampling point attending the respect of the hydraulic retention time of each

step. The samples were taken on March 23, 2010.

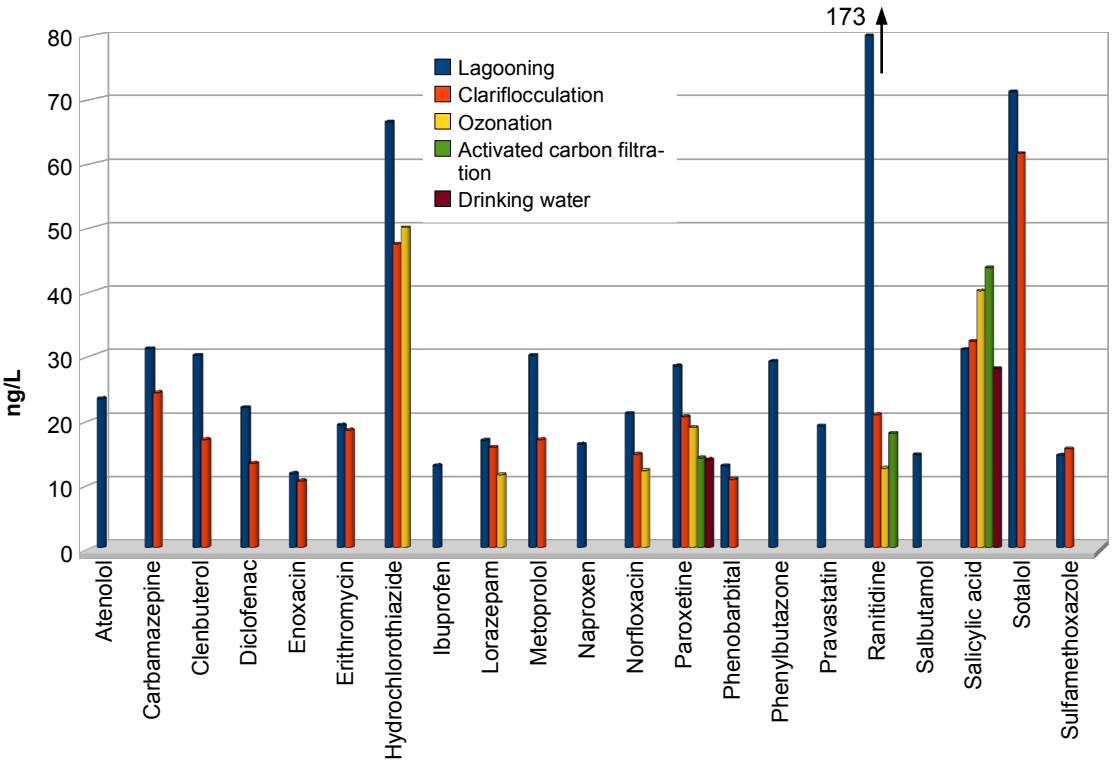


Figure 2.7.: Analysis of the different samples in Ferrara water works

Table C.5 and figure 2.7 shown the analytical results of all the samples taken on march 2010 after all the main water works step. In particular 21 compounds were detected with a maximum concentration of 173 ng L^{-1} (for the receptor antagonist Ranitidine) and the passage through the potable treatment plant of Ferrara guarantee a high removal rate of all compounds. In fact, if all the detected compounds are added the concentration pass from 694 ng L^{-1} after the lagooning step to 42 ng L^{-1} for the potable water where only 2 compounds were detected (the antidepressant Paroxetine and the analgesic Salicylic acid, commonly known as aspirin). It is also interesting to underline that, as reported from a lot of literature data (Broseus et al. (2009), Hua et al. (2006), Ikehata et al. (2006)), the conjugation from ozone and AC can rapidly degrade, transform and remove the PhCs from the water.

An important aspect to point out is about the increasing of the concentration of some compounds after the passage through the water works step. For example results about Ranitidine (report in table C.5, or in figure 2.7) shown that a clariflocculation may decrease the concentration of this substance from 173 to 21 ng

L^{-1} and ozonization till 12 ng L^{-1} but a passage through AC filtration cause an increase till 18 ng L^{-1}. This is probably due to the uncorrect calculation or the not exactly respect of the HRT but we are really talking about very small concentration of difference.

Analysis on bottle waters were made but in these samples PhCs were never detected.

2.6. Discussion

It is really difficult to discuss and compare all this different kind of waters, both for the different detected compounds and for the different water quality. In reality it is uncorrect to compare this different water matrix, but in order to understand what happens in the environment all the results are here reported.

Table 2.5.: Average and sum concentration of each sampling point (ng L^{-1})

Compounds	**GW**	**Po**	**Wells**	**Lag.**	**Clarifl.**	**Ozon.**	**AC filtr.**	**DW**
Detected, n	36	27	10	21	15	6	3	2
Average	106	28	34	33	23	24	25	21
Sum	2194	754	344	694	339	145	76	42

Table 2.5 try to compare the analytical results and to explain that the drinking water processes improve the water quality also towards PhCs. Table shows that GWs samples present a hight concentration of the detected PhCs. This is not a really problem because, comparing these results with the wells results it is clear, that a stationary situation, cause an accumulation of the pollutants in the GW. The continuous withdrawal of water, may decrease the concentration of the pollutant, as happened in the wells. Moreover, referring to the GW analysis (table C.3), it is clear, that all the concentration of these PhCs, is due to only 4 different compounds Indomethacine, Ketoprofen, Mevastatin and Doxycycline that, if summed, represents more than 70% of the total concentration. Perhaps in these particular points it is present a particular accumulation of these substances due to specific circumstances like stability, aerobic or anaerobic conditions.

The detected compounds decrease, passing from the GWs (36 compounds) to the Po River waters (27 compounds) until the wells waters (10 compound detected).

This means that, in general, the accumulation of the PhCs in GWs is possible but the aerobic, anoxic or anaerobic conditions in this particular sites can differ a lot and can vary from point to point.

Ying et al. (2008) for example conclude that PhCs are not likely to persist in an aerobic sand aquifer. The analyzed compounds in Ying et al. (2008) study were all degraded by GW microorganisms present in the aquifer tested under aerobic conditions. Contrasts between attenuation in GW or in a synthetic effluent and GW mixture were not consistent between PhCs. Some PhCs degraded the slowest in both aerobic microcosms and it appeared that exponential decay was inhibited beyond day 21. Under anoxic conditions, other PhCs were persistent over the time of the experiments, indicating that these compounds would not be likely to be removed into an aquifer where reduced redox conditions prevail within the storage zone.

CHAPTER 3

Hospital and Urban wastewaters

This chapter will present the real aim of this work, the hospital wastewaters, HWWs. Starting from a literature basis it will explain the problem connected with this kind of WWs compared with the *typical* UWWs, in order to understand the real differences between these two kind of effluents. Moreover, it will present the analytical results obtained in an experimental investigation carried out in two real hospital effluents.

The studied hospital structures were:

1. Lagosanto Hospital, a 300 beds hospital located near the town of Ferrara (30 km far)

2. Ferrara Hospital, the largest hospital in Ferrara, located near the town center and with a capacity of 900 beds

Normally HWWs are assimilated to UWWs in many countries where they are discharged into municipal sewage and collected to a WWTP where they are co-treated with urban or/and industrial effluents. This practice, considers that hospital and urban WWs are similar in terms of pollutants, concentrations and loads. Probably, this is not a correct assumption, because these WWs are really different.

Since 1980, this assumption has been often objected and rejected (Muylle (1980), Vanini and Gilli (1983), Pauwels and Verstraete (2006)), and analytical campaign

have been demonstrated that the two kinds of WWs presents really different qualitative and quantitative characteristics (Altin et al. (2003), Kosma et al. (2010), Liu et al. (2010), Verlicchi et al. (2010a), Verlicchi et al. (2010b)).

In fact daily HWWs flow rates range between 600-900 L bed^{-1} d^{-1} and so they are 2-5 times higher than urban flow rates which refer to one inhabitant equivalent (typically included in the interval 120-250 L $i.e.^{-1}$ d^{-1}).

Moreover, in hospital effluents, conventional pollutant (among them BOD_5, COD, SS) are in general higher than in UWWs, as well as micropollutants contents, such as PhCs, surfactants, mercury and others.

3.1. Sewage network in hospital structures

HWW is normally discharged directly, without pre-treatment, to sewers. Despite mostly being only a small fraction of the total WW volume in the influent of a WWTP, HWW has gained increasing scientific and public attention in the last decade. This is, in part due to the observation and expectation that HWW is a source for undesirable constituents, such as (multi-)antibiotic-resistant bacteria (Baquero et al. (2008), Kummerer (2004)). In other publications, the emission from hospitals was estimated for antibiotics, anaesthetics, disinfectants, heavy metals, AOX (Adsorbable Organic Halogens), iodised X-ray contrast media and cytostatic agents (e.g. Kummerer (2001)). The latter were also investigated in detail by Lenz et al. (2007b). Furthermore, a number of toxicity assays were performed (Boillot et al. (2008), Ort et al. (2010)). As a result, it has been suggested in some studies that pre-treatment of HWW prior to discharge into the sewers provides a reasonable solution (Gautam et al. (2007), Lenz et al. (2007b), Pauwels and Verstraete (2006)). However, this view is not unanimously supported. The separate treatment of HWW to reduce the development of resistant bacteria, was questioned (Kummerer (2009)): the substantial amount of antibiotics used outside of hospitals (in Germany more than 75%) seems to be a plausible reason, that resistant bacteria are also abundant in WW not receiving any HWW. Additionally, Boillot et al. (2008) found quantitatively far fewer microorganisms in the effluents of hospitals than in UWWs, which is consistent with other studies. With regard to pharmaceuticals,

Lenz et al. (2007b) report that 1) for some pharmaceuticals merely a small fraction of the amounts administered in the hospital were actually found in its effluent (i.e. 0.1-0.2% for doxorubicin, 0.5- 4.5% for 5-fluorouracil and 27-34% for total platinum) and 2) a complete onsite WWTP is needed to significantly remove targeted pharmaceuticals. This includes full physical and biological treatment steps, not only advanced processes. Capturing all sources within a hospital (wards, laboratories) may be further complicated by the fact, that different facilities discharge through different pipes to the common sewer. This particularly holds true for large existing hospital complexes.

Therefore, local circumstances need to be considered and the contribution of an individual hospital needs to be assessed in relation to the total load in a WWTP catchment. To our knowledge, only a few publications explicitly quantify pharmaceutical residues (subsequently referred to as *pharmaceuticals*) excreted within hospitals compared to the total pharmaceutical load in the corresponding STP influents (Feldmann et al. (2008), Heberer and Feldmann (2005), Thomas et al. (2007)). However, these studies are limited to a small number of pharmaceuticals, or make an assumption on the water flow instead of measuring the WWs flow, onsite to determine actual loads.

In general, a lot of hospital structures also in Italy are very old and many subsequent development of these structures made a situation with old sewage, different discharge point and unclear water flux. This involves that, for the oldest structures, a lot of discharge point may occurs in the local sewage network and mainly a lot of losses, due to the old hospital sewage, may cause a diffusion and a contamination of dangerous pollutant into the environment.

Old structures in Italy are made in the town center, where may be that also the local sewage are old and with a lot of losses. This situation can really represent an environmental problem for the local diffusion of a lot of pollutant and a lot of bacteria in the GWs.

These problems are overcome in those situation where hospital are built in new town, and in general in new context, where the local network are up-to-date and does not present any kind of losses. In general, in these context rain water are divided from WWs. This is an important aspect in order to avoid excessive dilution

of the WWs conveyed in public sewage and then at the WWTP.

For instance the two hospital structure studied in this research activities represent specific example of these concept. In fact, Ferrara Hospital is an old hospital built in the town center and this hospital presents different discharge point (at least 3) and it does not present a separate sewage for rain and for the specific producted WWs.

At the contrary, the new Lagosanto Hospital, built in recent years, has a new sewage and only one discharge point. Moreover, it presents a separate sewage for rain and for the produced WWs. In this case the management of the hospital effluents are really more easy than in the previous case, because the WWTP will treat only WWs and not rain waters, so the biological processes will be done with the correct concentration of biomass avoid dilution or washing with rain waters.

3.2. Nature of HWWs

It seems established that the microbial composition of the WWs produced by hospitals is similar to that of urban sewage with regard to bacterial contamination of fecal origin (Salmonella, *E. coli*), while differing in the presence of a greater number of micro-organisms responsible for hospital specific infections (*Pseudomonas* and *Staphylococcus aureus*).

With regard to the contamination of chemical and physical nature, HWWs are certainly different from UWWs (table 3.1).

Table 3.1.: Different content of HWWs compared with UWWs (Mersi et al. (1993))

Chemical	**Fisical**	**Biological**
Medicines	Radioactive marker	Bacterial load
Chemical reactives	Temperature	Antibiotic-resistant bacteria
Heavy metals		Pathogens
Disinfectants		
Sterilizing		

From a chemical point of view in a HWWs are certainly present:

- antibiotics, derived from the patient excretion
- chemical reactive, derived from the washing waters for the different wards

- disinfectants, derived from the cleaning for hygienic purposes of the wards

The physical contamination (mainly radioactive) may derived from the physiologic elimination from the patient treated with these compounds with therapeutic and diagnostic purposes.

Kummerer and Henninger (2003) explain that the majority of antibiotics used are only partially metabolized after administration, and are released via patient excreta into the municipal sewage system. Kummerer and Henninger (2003) say that the volume of antibiotics used in hospital and private households and released into the municipal sewage indicate a selection pressure on bacteria. In particular resistant bacteria could be selected by antibiotic substances present in the WWs. Steps should be taken to reduce the risk by proper handling of antibiotics and their residues both in hospitals and by private users.

Liu et al. (2010) speak about the SARS problem in China and explain that the presence of pathogenic microorganisms and viruses in HWWs is a major environmental and public health concern, especially following the outbreak of severe acute respiratory syndrome (SARS) in 2003.

3.3. Common management of HWWs, effects on public sewage

Hospital discharges represent a particular type of waste, due to the nature of the pollutants that are present in them: the active principles of drugs or metabolites, chemical reagents, heavy metals, disinfectants and sterilizing agents, radioactive markers, pathogens, antibiotic-resistant strains and viruses.

Antibiotics, cytostatic agents, anesthetics, disinfectants, heavy metals (platinum and mercury), rare elements (gadolinium, indium and osmium) have higher concentrations of a few orders of magnitude compared to those found in a UWWs (Kummerer (2001)), always in a range between the ng L^{-1} and μg L^{-1}.

From microbiological point of view, HWWs are similar to the urbans one for bacterial contamination of fecal type (Salmonella, Shigella, *E. coli*, etc.). A difference is about the major number of microrganisms responsable of the typical hospital infections (*Pseudomonas sup., Staphylococcus aureus*) and organisms with increased

resistance to antibiotics (from 2 to 10 times that found in UWWs) as reported in Pauwels and Verstraete (2006). Also the viral load is a quite different parameter from a quali-quantitative point of view. HWWs present a great number and wider range of species, especially where there is a department of infectious diseases.

Usually these discharges are treated as UWWs (Mersi et al. (1993)). After mild chlorination within the hospital, they are placed on public sewer and treated in combination with the urban and/or industrial WWs, made in accordance with current legislation, mainly in order to remove organic compounds of carbon, nitrogen and phosphorus: substances that come regularly and in large amounts (order of magnitudo of mg L^{-1}) to the system.

PhCs are present in concentrations lower than the conventional macropollutants. They include a wide range of compounds with different physical-chemical characteristics and therefore different behaviour and fate in the WWTP.

Solubility, volatility, molecular weight, biodegradability, polarity (lipophilicity or hydrophilicity), stability, life-time and persistence are the characteristics that determine the specific behaviour.

There are few studies that relate only to HWWs (Kummerer et al. (1997), Kummerer (2001), Emmanuel et al. (2001), Altin et al. (2003), Chiang et al. (2003), Wen et al. (2004), Pauwels and Verstraete (2006), Pauwels et al. (2006), Gautam et al. (2007)). These studies usually investigate the removal efficiency of the different systems regarding only a small group of pharmaceuticals compounds (only to name a few: Heberer (2002b), Ternes et al. (2004a), Andreozzi et al. (2005), Jones et al. (2005a), Castiglioni et al. (2006), Ternes and Joss (2006), Vieno et al. (2007a), Heberer and Feldmann (2005)). The substances under study are frequently dissolved, lipophilic, degradation and low volatility subsatnces.

Hospital discharges are the major source of pharmaceuticals or their metabolites in the WWTP, although for some drugs has been found that the urban contribution is similar or even greater than hospital one (Clara et al. (2004), Pauwels and Verstraete (2006) and Pauwels et al. (2006)). In addition, hospital may be a diffusion source for other dangerous substances like heavy metals. Kummerer et al. (1999) and Kummerer and Helmers (2000) for example talk about the diffusion in the aquatic environment of platinum and gadolinium deriving from hospital structures.

The strategies to reduce the presence of these substances are basically three:

1. optimize existing treatments,

2. implement measures for upgrading of existing facilities through new processes of ageing (end-of-pipe process),

3. separating the effluent at the source.

This approach is based on the idea of being able to obtain an effluent composition appropriate for a specific treatment and subsequent disposal (waste design). This involves the separation of the WWs at the source (source separation) and, where possible, a collaboration with the manufacturing industry (source control) to reduce (to zero) the release in the water cycle (initial contamination) (Larsen et al. (2004)).

Moreoever, the approach takes into considerations the concept that a lot of PhCs present a hight solubility, due to their chemical characteristics and, for this reason, they have the propensity to stay in the liquid phase (urine) and not in the solud one (faeces) (Ternes et al. (2004b), Ternes et al. (2003), Larsen and Gujer (1996), Lienert et al. (2007a), Lienert et al. (2007b)). For this reason, a source separation can improve the removal efficiency of a treatment, because the concentration of micropollutants can be higher. For more details about the source separation see paragraph 5.3.

The studies, that have been done on hospital wastes so far, have mostly focused on solid wastes. There have been quite detailed studies, especially on the collection, characteristics, determination of characteristics and disposal of infectious wastes. But only a limited number of detailed studies about complete WW treatment have been found. The studies done on HWWs dealed mostly with the treatability of the chemical materials used for the sterilization in these institutions. For instance, Matsushima (1988) has proved that these WW include a lot of disinfectants such as cresols, triclosan, chlorhexidine and benzalkonium, and pointed out that these substances have toxic effects in active sludge systems Altin et al. (2003).

As reported, the aim of this work is to study the HWWs characteristics and their different probable pollution impact on the environment. After a general study about the diffusion of PPCPs in the environment, in particular in surface waters and GWs,

but also in DWs, the attention is posed in the HWWs and in UWWs in order to compare their characteristics.

Leprat (1998) explains that the most frequent contaminants in HWWs are viruses and pathogenic bacteria (some of them are antibacterial resistant characters), molecules from unused and excreted non-metabolized pharmaceuticals (Halling-Sorensen et al. (1998)), organohalogen compounds, such as the halogenated organic compounds adsorbable on activated carbon (AOX) (Kummerer (2001)), radioisotopes (Erlandsson and Matsson (1978)).

Results on the microbiological characterization of HWWs (Leprat (1998)) reports that these effluents present a bacteria concentrations lower than the $10^8/100$ mL generally present in the municipal sewage system (Metcalfe and Eddy (1991)). The low most probable number (MPN) detected for fecal bacteria in hospital is probably due to the presence of disinfectants and antibiotics. Markers of viral pollution of water, such as enterovirus and other viruses have been identified in the hospital effluents.

Studies on the bacteria flora of hospital wastewater into WWTP have shown that bacteria acquired resistant character. Antibacterial resistancy is a threat to the efficacy of antibacterial substances. The development of resistance to antimicrobial agents by many bacterial pathogens has compromised traditional therapeutic regimens, making treatment of infections more difficult (Halling-Sorensen et al. (1998)).

Three factors have contributed to the development and spread of resistance: mutation in common genes that extend their spectrum of resistance, transfer of resistance genes among diverse microorganisms, and increase in selective pressures that enhance the development of resistant organisms (Halling-Sorensen et al. (1998), Davidson (1999), Schwartz et al. (2002)). Emmanuel et al. (2005b) explained that hospitals use a variety of chemical substances such as pharmaceuticals, radionuclides, solvents and disinfectants for medical purposes as diagnostics, disinfections and research (Erlandsson and Matsson (1978), Richardson and Bowron (1985), Kummerer and Al-Ahmad (1997)). After application, some of these substances and excreted non-metabolized drugs by the patients enter into the hospital effluents (Halling-Sorensen et al. (1998), Kummerer (2001)), which generally reach, as well as the UWWs (see Figure 3.1), the municipal sewer network without preliminary treat-

ment as reported in Leprat (1998).

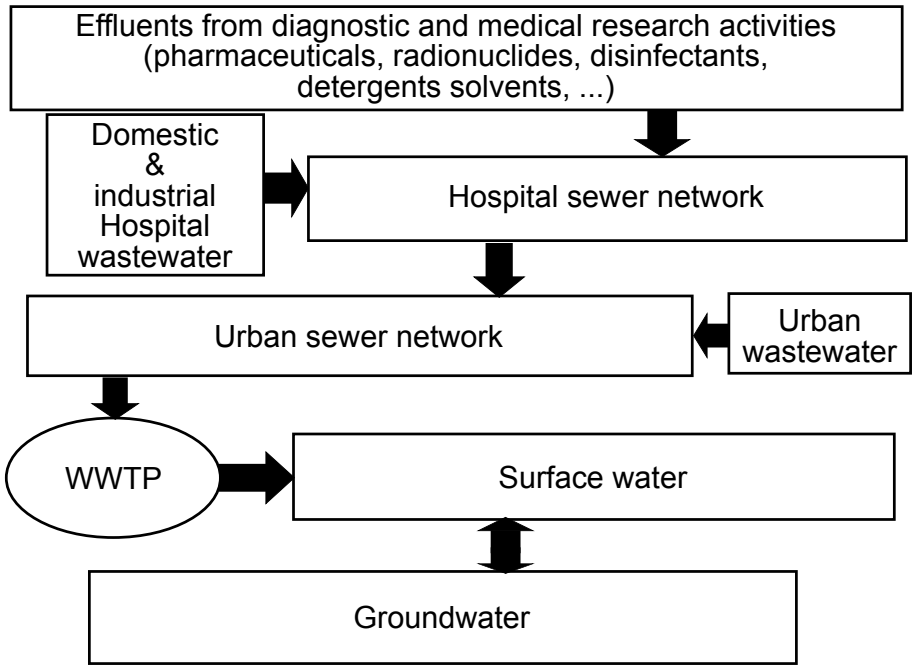


Figure 3.1.: Problems of hospital effluents, their impacts on WWTP and on natural environments (adapted from Emmanuel et al. (2005b))

The chemical substances used in hospitals for care activities and medical research are generally found in the WWs. Even if the high volume of generated WWs by these establishments, ensures an important dilution of the pollutants, the discharge of these effluents in the urban sewer network or in the natural environment generates risks for human health, and represents a significant contribution to the general contamination of the environment, and more particularly of the aquatic environments.

The most important pollutants present in HWWs are pathogenic microorganism, organohalogen compounds, such as the AOX (halogenated organic compounds adsorbable on activated carbon), radioisotopes , detergents and pharmaceuticals.

In Italy (but also in other part of the world) for HWWs are not prescribed particular and specific treatment. These waters are completely assimilated to the UWWs and in some cases this may represent a big environmental problem.

The main problem is about the dilution of the contaminants. If an hospital discharge his effluent in a public sewage all the WWs are collected in a WWTP. In this site the treatment is generally a biological treatment as activated sludge, designed for the removal of BOD_5 and SS, but not for pathogens (Liu et al. (2010), Koivunen et al. (2003), Chitnis et al. (2004)). In this case the dilution play an

important role. If a large hospital with 1000 beds, discharge in a large WWTP (with more than 100 000 i.e.), the diffusion of PhCs into the environment due to the low biological efficiency does not represent a relevant problem.

In Ferrara the largest hospital of the town (about 900 beds) discharge in the municipal WWTP where are collected all the WWs from the town and from the near industrial site for a treatment capacity of more or less 240 000 i.e. In this case HWWs are a small percentage (more or less 1%) of the total WWs presents in the WWTP and a biological treatment designed for the urban or industrial WWs is sufficient to minimize the hospital environmental impact.

In other cases where hospitals discharge in a small WWTP treated only UWWs the percentage of HWWs may be higher and the environmental impact is very different. For example if we consider Lagosanto Hospital, a small hospital with 300 beds that discharge in a small WWTP (about 5000 i.e.), in this case the percentage of HWWs varies from 10% to 15%.

HWWs contain a variety of toxic or persistent substances such as pharmaceuticals, radionuclides, solvents and disinfectants for medical purposes in a wide range of concentrations due to laboratory and research activities or medicine excretion. Most of these compounds belong to the so called emerging contaminants; quite often unregulated pollutants which may be candidates for future regulation depending on research on their potential health effects and monitoring of their occurrence. They include surfactants, PPCPs, EDC, illicit drugs, gasoline additives and many other groups of compounds. Their main characteristic is that they do not need to persist in the environment to cause negative effects, since their high transformation or removal rates can be compensated for, by their continuous introduction into the environment (Barcelo (2003)).

In recent years, increasing attention has been paid to the presence of emerging pollutants in WWs, surface waters and ground waters (Daughton and Ternes (1999), Heberer (2002a), Barcelo (2003), Daughton (2004), Petrovic et al. (2009)). Referring to PhCs, large amounts of different compounds are used worldwide and, in the last decade, their sales have been continuously increasing (Kummerer (2001), Ternes and Joss (2006), Jjemba (2006); Lienert et al. (2007a); USEPA (2009)).

After administration, the active substances of medicaments are metabolized, but

only to some extent. The unmetabolized active substances are excreted, largely in urine and partially in faeces, as unchanged substances, as a mixture of metabolites or conjugated with an inactivating compound attached to the molecule (Halling-Sorensen et al. (1998), Lienert et al. (2007a)), thus entering the water cycle.

Hospitals are important sources of these compounds, but they are not the only source: residues of pharmaceuticals can be found in all WWTP effluents, due to their inefficient removal by conventional systems (Kummerer (2001), Petrovic et al. (2003), Carballa et al. (2004), Onesios et al. (2009)). Despite their specific nature, quite often hospital effluents are considered to be of the same pollutant load as UWWs and are discharged into public sewer networks, collected to a WWTP and co-treated with UWWs.

The difficulties in removing micropollutants, especially PhCs, from WWs are due to the fact that their concentrations are in the range 10^{-3}-10^{-6} mg L^{-1}, which is much smaller than those of conventional macropollutants (BOD_5, COD, nitrogen and phosphorus compounds...). Moreover, they include a broad spectrum of compounds with great differences in their main properties which affect their behavior and fate in the WWTP: solubility, volatility, adsorbability, absorbability, biodegradability, polarity and stability. In addition, municipal WWTPs were first built, then upgraded, with the principal aim of removing carbon, nitrogen and phosphorus compounds, as well as microbiological organisms: pollutants which regularly arrive at the WWTP in concentrations to the order of mg L^{-1} and at least 10^6 MPN/100 mL. Conventional treatments are not designed to be able to greatly remove micro-contaminants as well.

Other Ph.D. thesis studies about hospital structures. For example in her Ph.D. thesis Wangsaatmaja (1997) studied a general medical hospital with 538 beds.

Some interesting data are the daily average water consumption (1034 m^3 d^{-1}) divided in hospital use with 1589 L bed^{-1} d^{-1} and dormitory purposes with a pro-capita consume of 517 L $head^{-1}$ d^{-1}. For the water consumption in Italy and the comments about this topic in my thesis see section 3.4.

Hazardous and Toxic Materials (HTM) Office Board of Public Works, Los Angles (1995) estimated that around 15 percent of hospital waste is contaminated with infectious agents potentially hazardous to human health such as hepatitis and human

immunodeficiency virus (HIV) and to the environment.

In Thailand, the characteristics of HWWs from 21 provinces was found to be that BOD_5, SS and pH were 113 mg L^{-1}, 103 mg L^{-1} and 7.17 respectively.

Wangsaatmaja's thesis reported a comparison between the WWs of two different hospital, the first in Indonesia and the second one in Thailand. She also reported all the analysis done about the principals macro parameter on the water. In particular, interesting dates are about COD, BOD_5, SS, P and N.

Figure 3.2reports the different water activities as reported in Wangsaatmaja (1997).

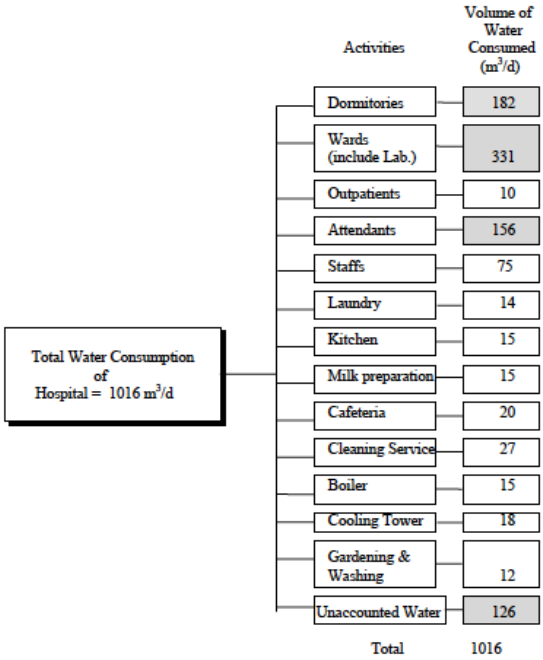


Figure 3.2.: Estimation of water uses in each activity (Wangsaatmaja (1997))

Water uses in each activity of the hospital treated in Wangsaatmaja (1997) has been calculated by different methods. It is possible to conclude that water consumption in the wards including the laboratories is the highest (331 m^3 d^{-1}) compared with other activities. It was surprisingly known that the attendants of this hospital have also consumed significant amount of water (156 m^3 d^{-1}) which is mainly for toilet purposes. Total number of attendants during observation were 2600 in a day. This is a unique case especially for a typical children's hospital where the patients are always accompanied by their parents during examination. Moreover, most of inpatient parents also stay in the hospital for 24 hours. Number of attendants are totally influenced by the number of patients.

For several, widely applied pharmaceuticals, an individual hospital seems to be a small additional point source in the catchment of a WWTP. In Ort et al. (2010) a hospital with 4.4 hospital beds per 1000 i.e. contributed less than 15% to the total load in the influent of the sewage treatment plant for 28 substances, detected in both hospital effluent and WWTP influent, which is in good agreement with estimates from other studies. Considering a conservative worst case uncertainty estimation, the hospital contribution only exceeded 15% for two substances, roxithromycin (max. 56%) and trimethoprim (max. 18%).

3.3.1. THM in WWs

Before entering into the municipal sewer, a chlorination is sometimes required for the whole HWWs flow rate, sometimes only for the effluent, from infectious disease wards (Emmanuel (2004)). The common practice of co-treatment of hospital and urban WWs, at a municipal WWTP is not considered an adequate solution by many authors (among them: Altin et al. (2003), Pauwels and Verstraete (2006), Vieno et al. (2007b)) because it is based on dilution of different discharges and does not provide a segregation or separation of pollutants, and in particular of emerging contaminants and toxic substances from the liquid phase which, is then discharged into the environment.

The widespread medical use of chlorine disinfection is due to its very broad spectrum of biocide activity against bacteria, virus and fungi and simple operation. However, this method is capable of producing undesirable disinfection by-products (DBPs), its efficacy depends much upon the quality of the feed water and in particular low efficiency of virus removal.

There is an increasing concern about the formation of mutagenic or carcinogenic and toxic disinfection by-products, that are potentially harmful to humans and aquatic organisms (Monarca et al. (2000)). Chlorine-containing disinfectant for virus removal, depends much upon the quality of the feed water. The results of study, indicate that viruses still can be detected, despite the lower than 50 PFU/100 mL number of *E. coli*, which accorded with the HWWs discharging standard (Emmanuel et al. (2004), Sun et al. (2006)) because of their much higher tolerance, compared to coliform or enteric pathogenic bacteria Wu et al. (1991).

Moreover, the presence of suspended solids and organic compounds in WWs, often makes disinfectants' efficiency to decrease drastically (Emmanuel et al. (2005a), Emmanuel et al. (2005b)). Therefore, many hospitals use excessive disinfectants to ensure thorough sterilization. In the investigation conducted in China by Liu et al. (2010), the highest residual chloride level in effluent was 128 mg L^{-1} and the second highest value was 103.50 mg L^{-1} (Cheng et al. (2004)). Statistical study showed that the overall emission of residual chlorine of these hospitals, was about 14 400 kg yr^{-1} in Jinan city, the capital of Shandong province (Cheng et al. (2004)).

Excessive residual chlorine not only increased the treatment costs of hospital wastewater, but also caused the serious second pollution to aquatic environment (Liu et al. (2010)).

A particular problem in HWWs treatment is the disinfection phase. The italian regulations prescribe a disinfection of the raw HWWs, before the discharge in public sewage. For this reason all the hospital need a chlorination plant, that have to guarantee a contact time of 30 mins, to respect the normative.

This prescription derives from an old law that considered the hospital liquid effluent dangerous for the human health for his hight presence of bacterials and virus.

This law, in these years, is under study with the objective, to delete it because a chlorination of a raw WW may have a high impact in the future treatments step. In particular, if the chlorination objective is to kill all the bacterial and the virus presents in this WW, the quantitative of this disinfectant may be very hight (more or less 10 times more than the ammonium concentration).

An important aspect correlated with this treatment is the formation, in the WWs, of many sub products derived from the chlorine, the trihalomethane (THM).

A lot of author are studying this important problem and an interesting study about the formation of THM in WWs after the chlorination is Matamoros et al. (2007b). In this work the authors compare three different chlorinated effluents adding different concentrations of chlorine dosage (2-5-16 mg L^{-1} of Cl_2). An important conclusion is that THM concentrations observed during the 2 year study period never exceeded quality standards applicable to drinking water.

Another important conclusion is about the role of ammonia in WWs to limit the presence of THM, in particular Ammonia nitrogen is a key factor in achieving

breakpoint chlorination, as its reaction with chlorine. Chlorine could react with organic compounds present in WWs, such as amino acids from complex organic matter, leasing to low THM formation.

In conclusion the presence of significant concentrations of ammonia nitrogen (in the absence of nitrification processes, so in a raw WWs) ensures that the risk of THM formation is significantly prevented.

3.3.2. The water body receptor

Another problem is about the final dilution in the environment. When a WWTP discharge in a large river the bioaccumulation of the PhCs does not represent a relevant problem.

For example Ferrara WWTP discharge in Volano river (an affluent of the Po River) that presents an average flow rate of 50 m^3 s^{-1}. The dilution is guarantee from this hight difference in the flow rate between the Volano river and the effluent of the WWTP (80-100 times lower).

This hight difference in the flow rate is not so important in a small WWTP that discharge in a small channel or river.

In the case of Lagosanto Hospital, this 300 beds hospital, convey its WWs in a WWTP treating 5000 i.e. and finally all the treated WWs are discharged in a small channel used in summer for irrigational uses, the dilution is not really guarantee. In the winter season, when agriculture does not need water, this channel is dry and the only water in this season comes from the WWTP.

This particular aspect is really important for the diffusion of PPCPs and other pollutants in the environment and in the food chain. In this case the aspect of bioaccumulation, not only in the animals, but also in the sludge or in the ground near the discharge is more relevant that in the first case and the environmental consequence will be monitored as also reported in Emmanuel et al. (2005b), EPA (1992), Fawell (2008).

An important parameter to greatly understand the diffusion in the environment of the emerging contaminants is the time of half life of each compound. If this time is short the environmental accumulation is not a big problem because the compound will degrade in a few time, but, if the half life is long the bioaccumulation and the

persistence in the environment could be a problem (Zuccato et al. (2008), Zuccato et al. (2010)).

Nevertheless the persistence of PhCs in the environment is a known aspect and biologists and other scientists will study this phenomenon.

3.4. Water consumption in Hospital structures

Hospitals require a significant quantity of water per day for the different purposes and services depending on the activities, which take place within the structure. The quantity of WWs produced in a hospital depends on different factors: bed numbers, hospital age, accessibility to water, general services present inside the structure (kitchen, laundry and air conditioning), number and type of wards and units, institution management policies and awareness in managing the structure in safeguarding the environment, climate and cultural and geographical factors. Not all the hospital presents all the specific uses listed above. For example, in the last years, kitchen and laundry are not presents in all the hospital structures, that outsource these services.

It is possible to divide the hospital water requirements in:

- production of steam for heating
- sterilization of reusable principals
- humidity environments
- use technology (eg cooling towers)
- civilian use (ie catering and sanitary)

There is not a clear correlation between specific hospital consumption (expressed as L bed^{-1} d^{-1}) and hospital size (that is bed numbers), as shown by the data reported in figure 3.3, which refers to hospitals in different countries around the world (C.T.C. (1994); Wangsaatmaja (1997); Laber et al. (1999); Chawathe and Fellow (2002); Altin et al. (2003); Mohee (2005); Rezaee et al. (2005); Sarafraz et al. (2007); Duong et al. (2008); Suarez et al. (2009); Emilia-Romagna (2009); Mesdaghinia et al. (2009)). In this graph, data are spread between 200 and 1200

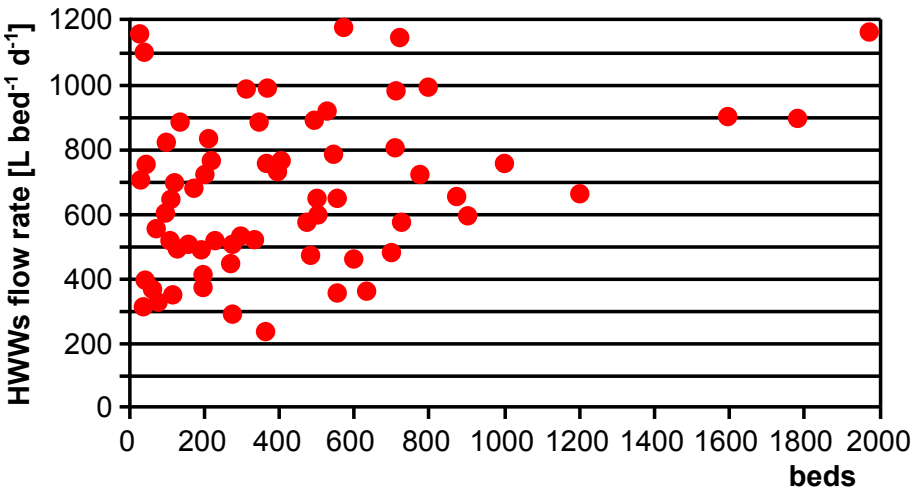


Figure 3.3.: Water consumption per day and per bed with respect to hospital size

L bed^{-1} d^{-1} with the highest values coming from industrialized countries and the lowest ones from developing countries, where the consumption keeps around 0.2-0.4 m^3 per bed and day.

Water consumption varies during the day: with respect to the daily average flow rate, increasing by up to +20% between 8 a.m. and 4 p.m. and decreasing to -30% between 1 a.m. and 8 a.m. Further differences occur during the year, with higher average values during hotter months (Joss et al. (2005); Mohee (2005); Boillot et al. (2008); Verlicchi et al. (2008)) in part due to irrigation. Peaking coefficients for hospital flow rates are quite similar to those generally assumed for the influent to a small WWTP (< 10 000 population equivalent, p.e.) as reported in Tab. 3.2 (Mersi et al. (1993); Frangipane and Pastorelli (1997)).

Table 3.2.: Peaking coefficient for hospital and urban effluents

Peaking coefficient	**Hospital effluent**	**Urban effluent**
Monthly	1.5-1.8	1.2-2
Daily	2-2.8	2-5
Hourly	3.5-4	3-4

Commonly adopted values for water consumption in urban centres are in the range of 150-300 L i.e^{-1} d^{-1} for industrialized areas, and 50-100 L i.e.$^{-1}$ d^{-1} for developing countries. Further literature data for specific water consumption (L pro capita^{-1} d^{-1}) for commercial, institutional and recreational sources show that the rate for hospitals is much greater than other specific consumption and that it ranges over a

wider interval (Metcalfe and Eddy (1991)).

In case of co-treatment, hospital effluent flow rate represents a percentage of the total WWTP influent flow rate whose value depends on hospital size (small with < 300 beds, medium with 300-700 beds and large with > 700 beds) and resident population in the urban centre. The situation is depicted in Figure 3.4, where the curves of hospital flow rate and urban one are drawn versus number of beds or population equivalent.

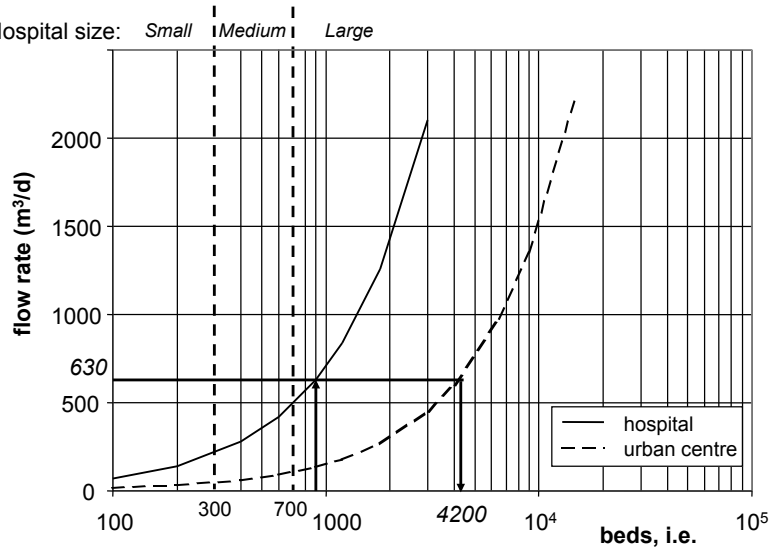


Figure 3.4.: Flow rates for hospital and urban centres of different size

These flow rates are based on a specific water consumption of 700 L bed^{-1} d^{-1} for hospitals and 150 L i.e.$^{-1}$ d^{-1} for resident populations. A large hospital of 900 beds, producing a daily flow rate equal to 630 m^3 d^{-1}, has the same hydraulic load as an urban centre of 4200 i.e. If this hospital is placed in a large town (for instance 100 000 i.e., 15 000 m^3 d^{-1}) and its effluent is co-treated at the same WWTP, the hospital flow rate corresponds to $\frac{630}{630+15000} \cdot 100 = 4\%$ of the total WWTP influent. Instead, if the same hospital effluent is collected to a small WWTP receiving UWWs from a 2000 i.e. urban centre (300 m^3 d^{-1}), its percentage on the total WWTP influent flow rate increases to $\frac{630}{630+300} \cdot 100 = 68\%$.

Figure 3.5 shows the hospital monthly consumption expressed in L bed^{-1} day^{-1}, for the Rimini Hospital, a structure that present 464 bed plus 83 day hospital bed (in total 547 bed). The monthly water consumption in m^3 month^{-1} are reported in table 3.3 for the 2008.

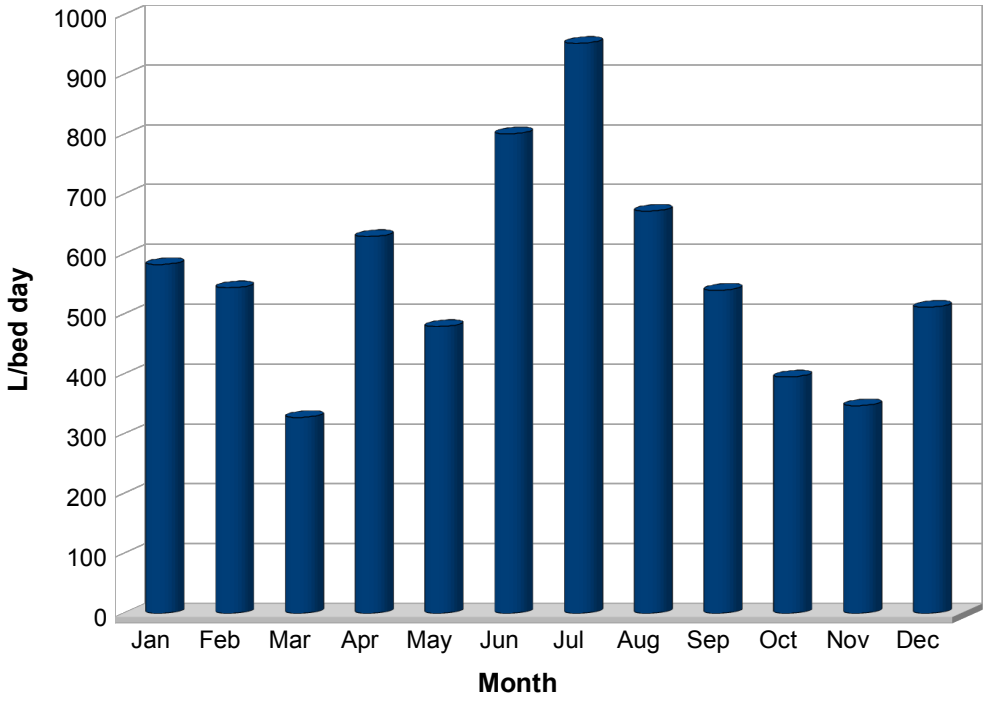


Figure 3.5.: Monthly Rimini Hospital water consumption L bed^{-1} day^{-1}

Table 3.3.: Monthly Rimini Hospital water consumption in m^3 $month^{-1}$

Month	**m^3 $month^{-1}$**
Jan	9887
Feb	8335
Mar	5557
Apr	10335
May	8129
Jun	13151
Jul	16153
Aug	11400
Sep	8864
Oct	6702
Nov	5698
Dec	8676

3.5. Characteristics of HWWs and UWWs

This section will describe the characteristics and the differences between the two kind of studied effluents, hospital and urban. All the results here reported made from a literature review. For the the experimental results about this topic see section 3.6.

3.5.1. Macropollutants

An in-depth literature review has been conducted on conventional pollutants of WWs from hospitals of different sizes (60-900 beds), different wards and of the following countries: France, Turkey, India, Iran, Italy, Thailand, Canada and Greece (Nardi et al. (1995); Kummerer et al. (1997); Wangsaatmaja (1997); Laber et al. (1999); Emmanuel et al. (2001); Altin et al. (2003); Chiang et al. (2003); Emmanuel (2004); Brown et al. (2006); Pauwels and Verstraete (2006); Kajitvichyanukul and Suntronvipart (2006); Gautam et al. (2007); Machado et al. (2007); Sarafraz et al. (2007); Tsakona et al. (2007); Verlicchi et al. (2008); Mesdaghinia et al. (2009)). Collected data for BOD_5, COD and SS have been elaborated, resulting in the curves of cumulative frequencies of occurrence (see figures 3.6, 3.7, 3.8). The grey bands in the three graphs represent the variability ranges for each cumulative frequency curve. Corresponding average values for BOD_5, COD and SS in HWWs and medium strength UWWs are reported in table 3.4, along with the resulting ratios. Referring to these three parameters, and by considering their usual concentrations in the influents to municipal WWTPs, it can be observed that in HWWs BOD_5, COD and SS keep 2-3 times higher than in UWWs.

The specific contributions for each patient are reported in table 3.4 where are compared with the typical inhabitant equivalent (Metcalfe and Eddy (1991)). Hospital values corresponding to about 2-3 times urban values.

Table 3.4.: Average values in HWWs and UWWs. Data expressed in g i.e.$^{-1}$ day^{-1}

Parameter	**HWWs**	**UWWs**	**Ratio**
BOD_5	160-200	60	2.6-3.3
COD	260-300	100-120	2.5-3
SS	120-150	70-90	1.8-2.3

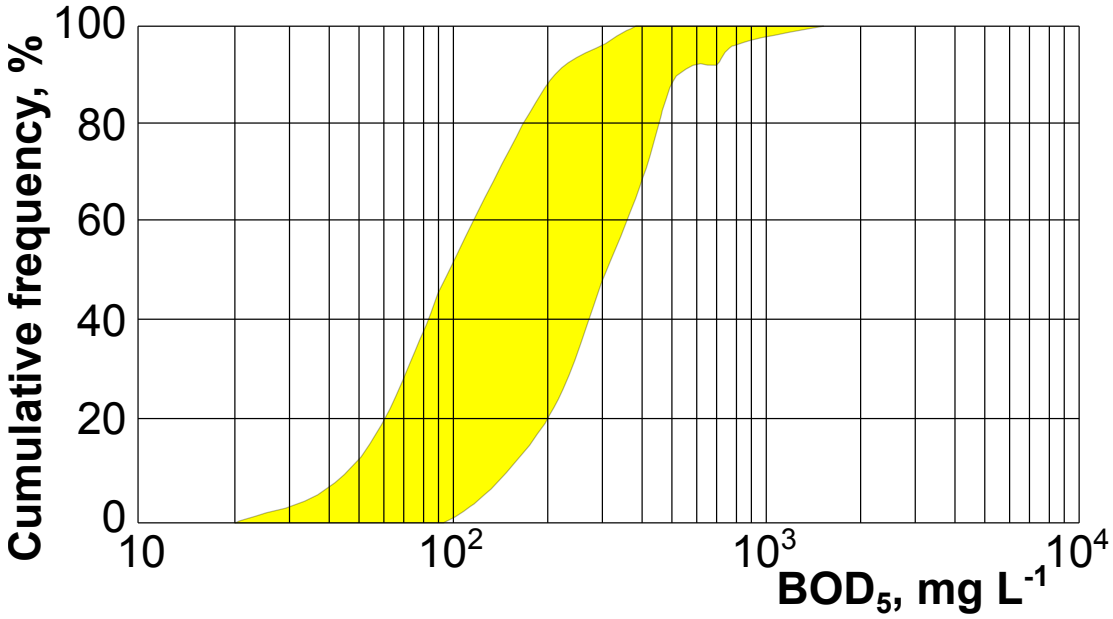


Figure 3.6.: BOD_5 cumulative frequency curves in HWWs and UWWs

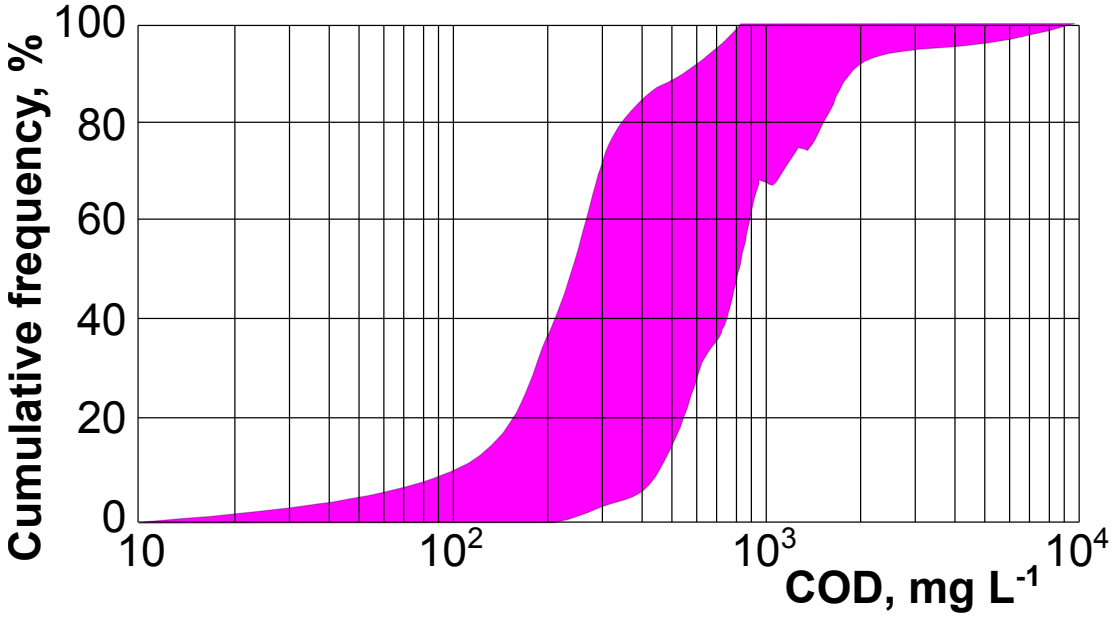


Figure 3.7.: COD cumulative frequency curves in HWWs and UWWs

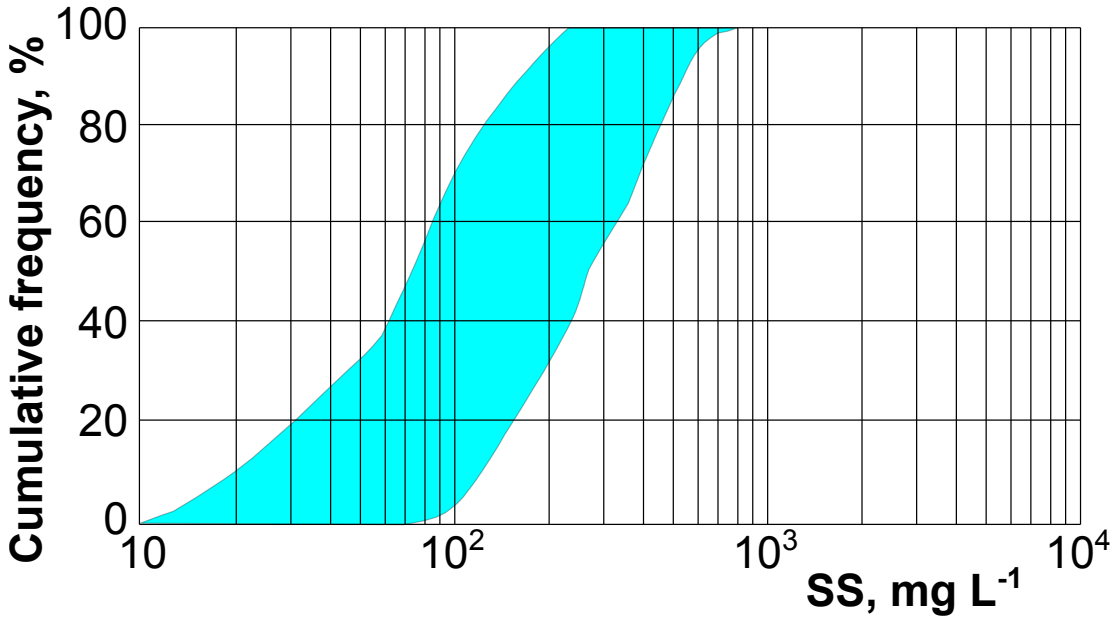


Figure 3.8.: SS cumulative frequency curves in HWWs and UWWs

As for other common macropollutants, typical ranges of variability as well as average concentrations in HWWs and UWWs as derived from an analysis of the literature data are reported in table 3.5, (Metcalfe and Eddy (1991); Nardi et al. (1995); Laber et al. (1999); Altin et al. (2003); Emmanuel (2004); Wen et al. (2004); Rezaee et al. (2005); Gautam et al. (2007); Sun et al. (2008); Boillot et al. (2008); Verlicchi et al. (2008)). The ratio between the average concentrations in HWWs and UWWs is reported in the last column. It is less than 1 for all the parameters with the exception of chlorides, which are found in higher concentrations in HWWs than UWWs.

3.5.2. Micropollutants

A great variety of chemical substances are commonly used in hospitals for laboratory and research activities, in particular surgery. These not only include pharmaceuticals, but also diagnostic agents and disinfectants. Consumption, use and application of pharmaceuticals may vary considerably with time. Annually, changes in quantity and quality of medicaments may result due to new legislation, the introduction of new active pharmaceutical ingredients or the disappearance of others following medical progress. Consumption may also differ from country to country (Schuster and Hadrich (2008)). The main classes of compounds used in hospitals are reported in

Table 3.5.: Other macropollutants with their typical values in HWWs and UWWs

Parameter	**HWW**		**UWW**	
	Ranges	**Average**	**Ranges**	**Average**
pH	7.7-8.1	8	7.5-8.5	7.5
Redox pot. mV	850-920	890		100
TKN mg L^{-1}	5-80	33	20-70	
Total P mg L^{-1}	0.2-13	4	4-10	7
Fat and oil mg L^{-1}	5-60	25	50-100	75
Chlorides mg L^{-1}	65-360	200	30-90	50
Surfactants[a] mg L^{-1}	3-7.2	4.5	4-8	5
E. coli MPN/100 mL	10^3-10^6	10^4	10^6-10^7	10^5
FC[b] MPN/100 mL	10^3-10^7	10^5	10^6-10^8	10^7
TC[c] MPN/100 mL	10^5-10^8	10^6	10^7-10^10	10^8

[a]Total Surfactants; [b]Fecal Coliforms; [c]Total Coliforms

table 3.6 (Kummerer (2001); Ternes and Joss (2006); Schuster and Hadrich (2008)), other groups of compounds are listed in table 3.7.

Table 3.6.: Main classes of compounds used in hospitals

Class	**Examples**
Antibiotics	cefazolin, chlortetracycline, ciprofloxacin, coprofloxacin, doxycycline, erythromycin, lincomycin, norfloxacin, ofloxacin, oxytetracycline, penicillin, sulfamethoxazole, tetracycline, trimethoprim
Analgesics and antinflammatories	codeine, diclofenac, dipyrone, ibuprofen, indomethacin, ketoprofen, mefenamic acid, naproxen, paracetamol, propyphenazone, salycilic acid
Cytostatics	5-fluorouracil, ifosfamide
Anaesthetics	propofol
Disinfectants	triclosan, glutaraldehyde
Rare earth elements	gadolinium
Heavy metals	platinum, mercury
Iodized contrast media (ICM)	iopromide, iopamidol

The type and amount of pharmaceuticals in HWWs reflect the substances and quantities of the particular drugs being administrated there. In the case of out-patients, unmetabolized pharmaceuticals excretion will partially occur inside the hospital with the remainder elsewhere, depending on the specific therapy and the time spent at the hospital. For example, cytostatics are administrated at high percentages in out-patients' treatment wards, but relevant amounts of them can also be found in the wastewater of in-patient treatment wards (Kummerer and Al-Ahmad (1997); Kummerer et al. (1999); Lenz et al. (2007a)). Gadolinium, which is used in magnetic resonance imaging (MRI), is 90% excreted during the hospital stay (Kummerer and Helmers (2000)). For total invasive anaesthesia, alkylphenol compounds are the most used, propofol in particular. These are characterized by a high rate of excretion, on average 90% (Kummerer (2001)).

Disinfectants are used in large quantities for the disinfection of surfaces, instruments and skin, in glue and size production and use, and in food processing. They are often highly complex products or mixtures of active substances: alcohols and aldehydes as well as chlorine-containing compounds such as recalcitrant chlorophe-

Table 3.7.: Other classes of compounds used in hospitals

Class	**Examples**
Psychiatric drugs, antidepressants, anticonvulsants	carbamazepine, gabapentin, phenytoin, valproic acid
Antihistamines	ranitidine, cimetidine
Antihypertensives	diltiazem
Antidiabetics	glibenclamide
β-blockers	atenolol, metroprolol, propranolol, solatolol
Hormones	17-β-estradiol, estriol, estrone, ethinylestradiol
Diuretics	furosemide, hydrochlorothiazide
Lipid regulators	atorvastatina, bezafibrate, clofibric acid, gemfibrozil, pravastatin
Stimulants	caffeine
Musks and fragrances	tonalide, galoxolide

nols which are used as active compounds. Solutions containing glutaraldehyde are still used in some hospital departments to disinfect reusable fiber-optic endoscopes, however, in general there is a tendency to substitute it with other compounds with a lower environmental impact.

The main heavy metals found in HWWs are platinum, due to excretions by oncological patients treated with cis-platinum and carboplatinum or other cytostatic agents; mercury, usually found in diagnostic agents, active ingredients of disinfectants as well as in diuretic agents and gadolinium, which is used in MRI due to its high magnetic moment. Following administration, the organic complexes are very quickly excreted unchanged. ICM exhibit a high biochemical stability and, hence, are excreted mainly unmetabolized (above 90%). They derive from X-ray examinations and radiological practices and consequently, their occurrence increases on weekdays (Ternes and Hirsch (2000)).

Finally, adsorbable organic compounds (commonly called AOX) are compounds which are the most persistent in the environment, and which tend to accumulate in the food chain; often they are toxic to humans and aquatic organisms. Some pharmaceuticals and their metabolites, may contain organic bound halogens and, therefore, contribute to AOX emissions. In clinical wastewaters, the main contributors to the burden of total AOX are ICM. Furthermore, the release of solvents used in laboratories, disinfectants, cleaning products and drugs containing chlorine, contribute to a lesser extent (Gartiser et al. (1996); Kummerer et al. (1998)).

Figures 3.9 (data from: Ohlsen et al. (2003); Gomez et al. (2006); Thomas et al. (2007); Foster (2007); Duong et al. (2008); Seifrtova et al. (2008); Lin and Tsai (2009); Suarez et al. (2009)) and 3.10 (data from: Kummerer et al. (1997); Kummerer et al. (1998); Kummerer et al. (1999); Kummerer (2001); Mahnik et al. (2007); Thomas et al. (2007); Foster (2007); Lenz et al. (2007b); Lenz et al. (2007a); Pauwels et al. (2008); Verlicchi et al. (2008); Weissbrodt et al. (2008); Suarez et al. (2009)) report literature data of pharmaceuticals concentrations and other emerging pollutants in hospital effluents, while figures 3.11 (data from: Golet et al. (2002); Golet et al. (2003); D'Ascenzio et al. (2003); Carballa et al. (2004); Joss et al. (2005); Khan and Ongerth (2005); Lindqvist et al. (2005); Xia et al. (2005); Nakada et al. (2006); Yu et al. (2006); Foster (2007); Gomez et al. (2007); Kim and Aga (2007); Matamoros and Bayona (2006); Matamoros et al. (2007c); Matamoros et al. (2007a); Matamoros et al. (2008); Radjenovic et al. (2007); Radjenovic et al. (2009); Ternes and Joss (2006); Thomas et al. (2007); Santos et al. (2007); Gulkowska et al. (2008); Huerta-Fontela et al. (2008); Spongberg and Witter (2008); Choi et al. (2008); Terzic et al. (2008); Gros et al. (2009); Ghosh et al. (2009); Kasprzyk-Hordern et al. (2009)) and 3.12 (data from: Kummerer et al. (1997); Kummerer et al. (1998); Kummerer et al. (1999); Kummerer (2001); Rule et al. (2006); Foster (2007); Oliveira et al. (2007); Mahnik et al. (2007); Thomas et al. (2007); Verlicchi et al. (2008); Weissbrodt et al. (2008); Suarez et al. (2009)) show those found in UWWs entering a municipal WWTP. Compounds are grouped into the different therapeutic classes (analgesics, antibiotics, anticonvulsants, cytostatics, hormones, β-blockers, ICMs, antihypertensives, antihistamines and lipid regulators) or according to the persistent substances or elements they contain (AOX and heavy metals) or according to their function (detergents/antiseptics). In addition, the stimulant *caffeine* and two common fragrances (tonalide and galaxolide) are reported and compared in the two kinds of WWs.

The literature data reported in these graphs generally refer to 24 h composite water samples, thus giving the corresponding average values of the micropollutant concentrations over the course of the day, *equalizing* the highest and lowest values of their instantaneous concentrations during the 24 hours. It is worth noting that (i) there is more literature data for UWWs than for HWWs. This is also due to the fact

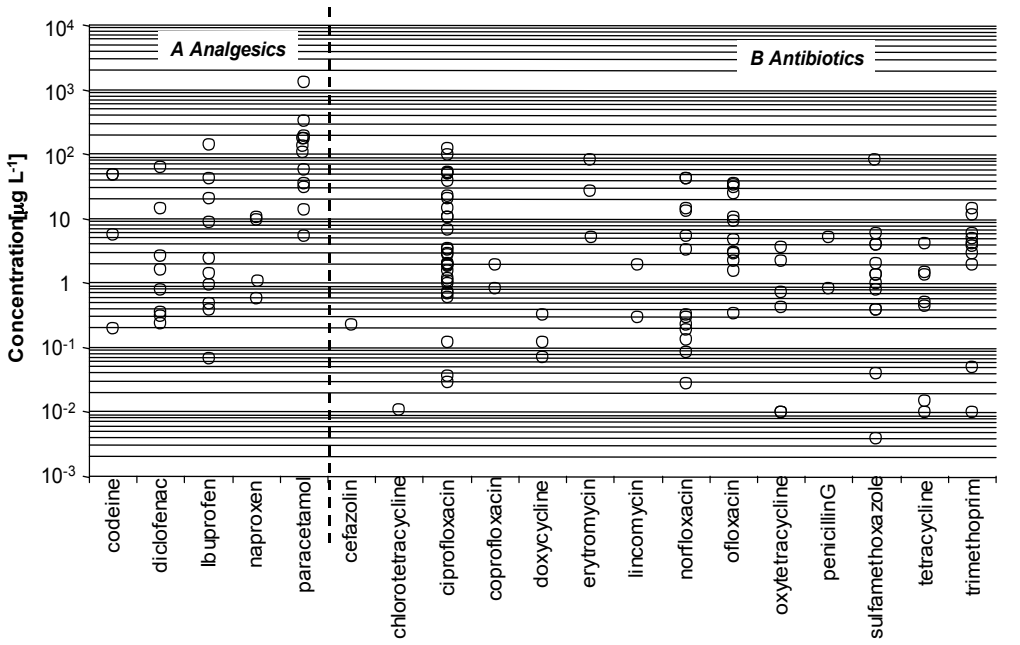


Figure 3.9.: Analgesics and antibiotics in HWWs

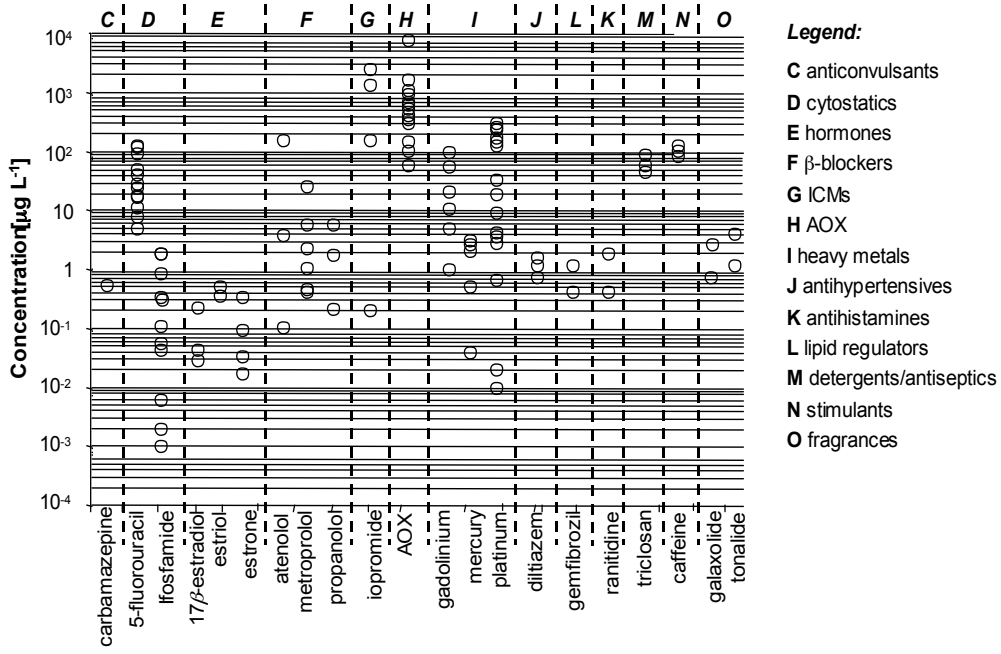


Figure 3.10.: Other emerging contaminants in HWWs

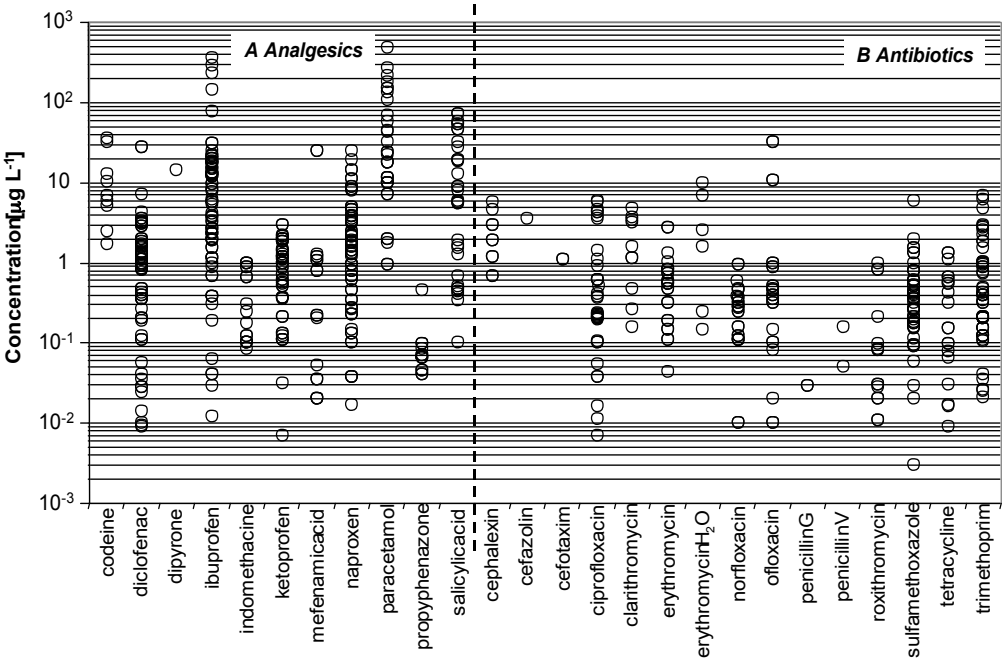


Figure 3.11.: Analgesics and antibiotics in UWWs

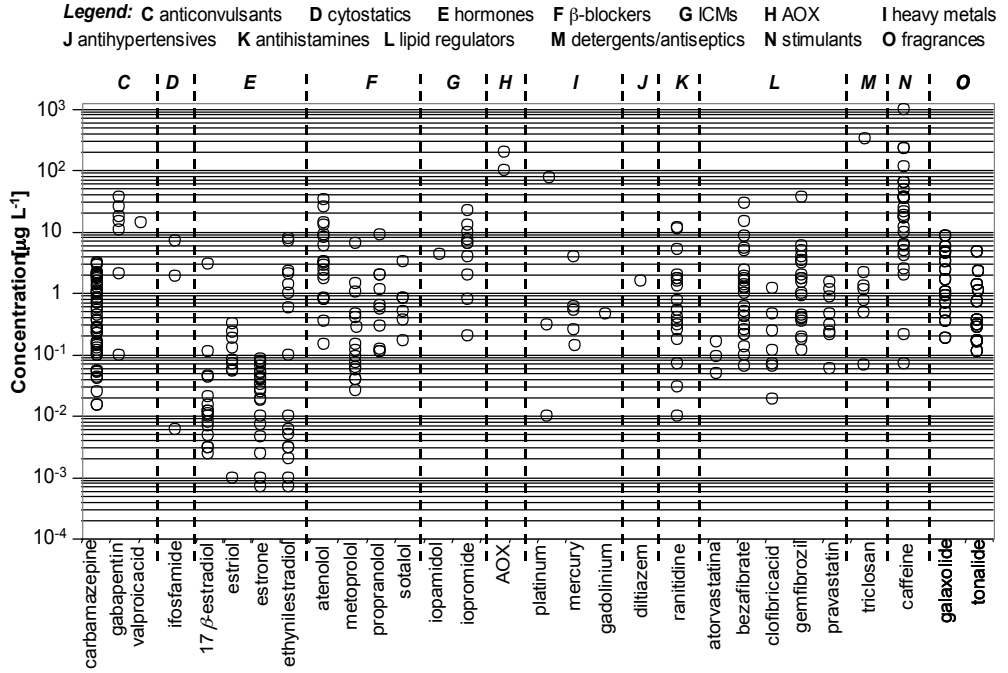


Figure 3.12.: Concentrations of other classes of emerging contaminants in UWWs

that quite often it is difficult to obtain permission to make analytical investigations on hospital effluents; (ii) for many compounds, the variability ranges are wider for HWWs than for UWWs, as are the corresponding highest values. Using all the collected data, (the expected) average concentrations for the different classes of compounds were found. These are reported in table 3.8. Average concentrations in HWWs are about 2-150 times the corresponding average concentrations in UWWs.

Table 3.8.: Ranges and average concentrations for the main classes of micropollutants in HWWs and UWWs (μg L^{-1})

Therapeutic class	**HWWs**	**UWWs**	$\frac{HWWs}{UWWs}$
Analgesics	100	11.9	8-15
Antibiotics	11	1.17	5-10
Cytostatics	24	2.97	4-10
β-blockers	5.9	3.21	1-4
Hormones	0.16	0.1	1-3
ICM	1008	6.99	70-150
AOX	1371	150	7-15
Gadolinium	32	0.7	35-55
Platinum	13	0.155	60-90
Mercury	1.65	0.54	3-5

3.5.3. PhCs concentrations over the course of the day

Figures 3.13 and 3.14 show the concentrations of some pharmaceutical compounds in instantaneous HWWs samples. For most compounds, measured concentrations keep quite low during the night and exhibit several peaks in the morning. as well as in the afternoon, following different consumption and excretion patterns (Kummerer et al. (1998); Kummerer et al. (1999); Kummerer and Helmers (2000); Joss et al. (2005); Duong et al. (2008)). These significant discrepancies, with respect to the corresponding daily average value, confirm that analytical investigations on pharmaceutical compounds, must be performed on 24 hour composite water samples in order to measure average concentrations for the different compounds, which would better represent the potential impact of the HWWs.

Figure 3.15 shows that the diurnal variation pattern of several compounds is paralleled by the nitrogen load, suggesting that human excretion is a major source of PhCs in WWs. The fragrances studied (AHTN and HHCB) also show quite a

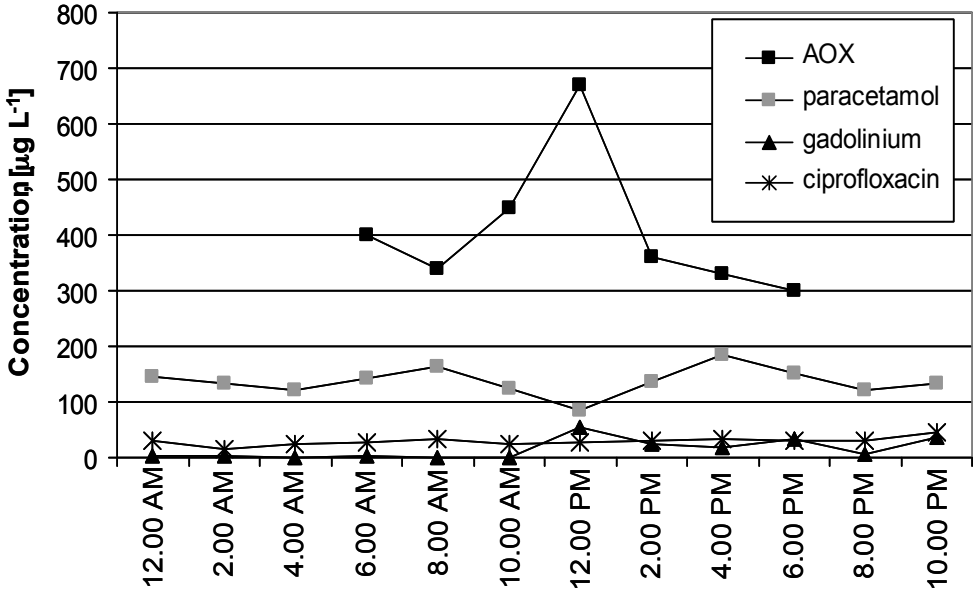


Figure 3.13.: Concentrations of some pharmaceuticals in a hospital effluent during the daytime

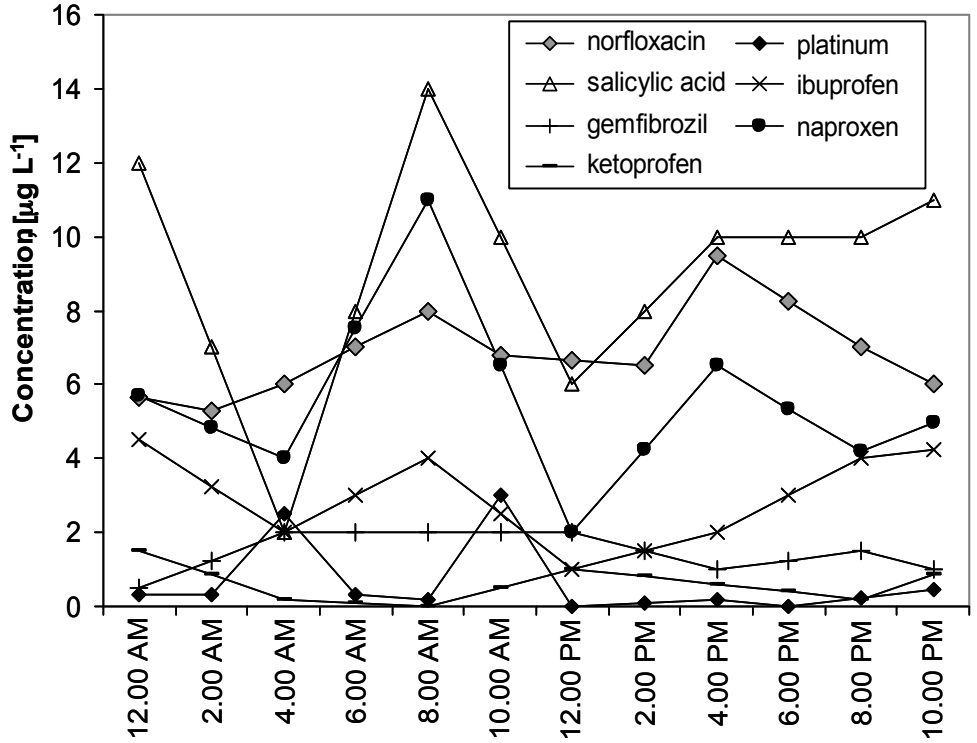


Figure 3.14.: Concentrations of some pharmaceuticals in a hospital effluent during the daytime

similar daily variation pattern (Joss et al. (2005)).

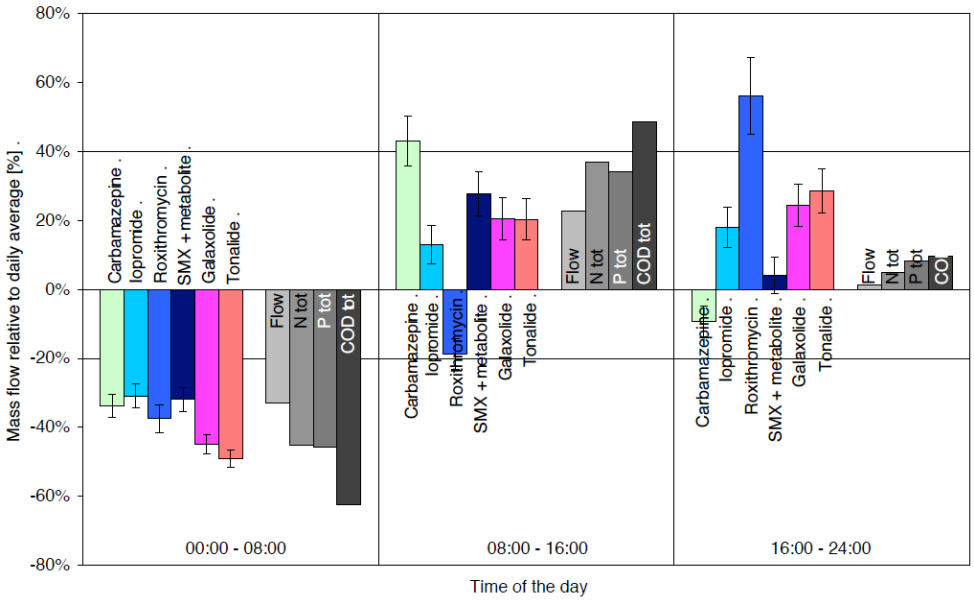


Figure 3.15.: Diurnal variation of the influent load from Joss et al. (2005). The 8-h composite samples show a similar relative variation as the flow rate or the loads of nitrogen (Ntot), phosphorus (Ptot) or chemical oxygen demand (CODtot). The mass flow is expressed as a relative difference to the 24 h average

3.5.4. Hospital contribution on PhCs load

Table 3.9 taken from Beier et al. (2011) shows a mass balance reporting the proportion of PhCs originating from hospitals in the UWWs.

Table 3.9.: Proportion of PhCs originating from hospitals in the UWWs

Substance	**Therapeutic use**	**From the hospital (%)**
Bezafibrate	Lipid reducing drug	27
Bisoprolol	Beta blocker	8-9
Carbamazepine	Anticonvulsant drug	3-8
Clarithromycin	Macrolide antibiotic	61-94
Ciprofloxacin	Antibiotic	19-36
Diclofenac	Anti-inflammatory drug	7-9
Ibuprofen	Anti-inflammatory drug	3-7
Metronidazole	Antibiotic	84
Moxifloxacin	Antibiotic	34-42
Tramadol	Analgesic	6-8

Table 3.10.: Comparison between the proportion of PhCs (in percentage) originating from hospitals in the UWWs showed in Beier et al. (2011), Ort et al. (2010) and this study in Ferrara

Substance	**Beier et al. (2011) 342 beds**	**Ort et al. (2010) 190 beds**	**This study 900 beds**
Carbamazepine	3-8	0-1.3	3
Diclofenac	7-9	1	2
Ibuprofen	3-7	2.7-8.5	4
Tramadolol	6-8	1.2-6	–

As shown in table 3.10 the hospital dimension plays a significant role in the percentage of the total PhCs originated from hospital structures.

3.6. Results of experimental investigations on HWWs

The WWs collected from two different hospitals were analysed in order to characterize and understand the effective proprieties of HWWs. In particular Lagosanto Hospital and Ferrara Hospital were the two structures under studying.

Lagosanto Hospital is a 300 beds structure placed 30 km far from the town of Ferrara and it presents different wards. Actually the WWs derived from this hospital are collected and discharged into a public sewage. These effluents are mixed with the UWWs derived from the near town (about 5000 i.e.), co-treated in a common conventional activated sludge (CAS) system and discharged in a small channel used in agriculture.

Ferrara Hospital, located near the town center, instead, is a large hospital with 900 beds. The difference with Lagosanto Hospital beyond the different size of the hospitals (300 beds versus 900) is due to the different capacity (230 000 i.e.) of the final WWTP where HWWs and UWWs are co-treated.

All the samples were taken in dry season in a litre plastic bottle and immediately prepared for the analysis. When the analysis were done in more time, all the samples were refrigerated at -20 ^{o}C. For the analytical methods in these WWs samples the techniques are reported in appendix A.

Tables 3.11 and 3.12 report the data of the different samples taken at the exit

of the two hospital before the chlorination step. The first step of this study was made in august/september 2009 and the second part (only in Ferrara Hospital) on march 2010 in order to compare the possible differences in the concentration of PhCs analysed due to the seasons.

In the first part of this experimentation (august september 2009) six samples were collected, four in Lagosanto Hospital and two in Ferrara Hospital. In the second part (march 2010) only the three samples in Ferrara HWWs were analysed.

In any case all the samples were taken in the middle of the week (Tuesday, Wednesdy and Thursday) in order to avoid peak (in positive or in negative) in water consumption and in the consequent PhCs concentrations. In fact it is possible that on Monday (or on Friday) the water consumption vary due to the presence of the week end, because in an hospital structure many patients, with no relevant pathologies, could go home in these days.

All the water samples in these two study phases were 24 hours samples collected with an autosample in order to obtain a representative sample of all the day and they were taken in dry period to avoid rain dilution.

Table 3.11.: Sampling date and day for Lagosanto analytical campaign in august and september 2009

	1^{st} sample	**2^{nd} sample**	**3^{th} sample**	**4^{th} sample**
Date	August, 25	August, 26	August, 27	September, 1
Day	Tuesday	Wednesday	Thursday	Tuestay

Table 3.12.: Sampling date and day for Ferrara analytical campaign in september 2009 and march 2010

	1^{st} sample	**2^{nd} sample**	**3^{th} sample**	**4^{th} sample**	**5^{th} sample**
Date	September, 2	September, 3	March, 16	March, 17	March, 18
Day	Wednesday	Thursday	Tuesday	Wednesday	Thursday

3.6.1. Lagosanto Hospital

The large number of analysed compounds (the 73 reported in table 2.1) and the large number of detected PPCPs in this kind of WWs (table C.6) cause a really difficult in the comment of these results.

Table C.6 reports the concentration in the four samples for the 59 detected compounds. Ofloxacin (antibiotic), Furosemide (diuretic), Ciprofloxacin (antibiotic) are the three compounds detected with the highest concentration.

On average the concentration of the detected compounds in this hospital are quite constant, both for the average concentration, ranging from 1631 to 1918 ng L^{-1}, and for the sum concentration, variable from 84420 to 97842 ng L^{-1}.

Table 3.13 shows the average, the standard deviation and the frequency of occurrence in the four samples taken in Lagosanto Hospital. For the complete analytical results see table C.6 at the appendix C.

Table 3.13.: Analytical results on Lagosanto WWs. Average (ng L^{-1}), Standard Deviation (SD) and frequency of occurrence with n=4

Compounds	**Average**	**SD**	**Frequency**
Acetaminophen	4533	1204	100
Atenolol	5131	1180	100
Atorvastatin	83	19	100
Azithromycin	60	69	50
Betaxolol	15	4	75
Bezafibrate	946	1349	100
Butalbital	22	13	75
Carbamazepine	733	105	100
Chlortetracycline	38	22	100
Cimetidine	26	5	100
Ciprofloxacin	11768	2124	100
Clarithromycin	59	52	100
Clofibric acid	23	17	75
Codeine	361	75	100
Diclofenac	304	118	100
Doxycycline	173	73	100
Enalapril	201	50	100
Enoxacin	410	60	100
Erithromycin	165	111	100
Famotidine	162	96	100

Fenofibrate	19	11	50
Fluoxetine	18	–	25
Furosemide	14378	3081	100
Gemfibrozil	19	1	100
Glibenclamide	75	21	100
Hydrochlorothiazide	1748	432	100
Ibuprofen	1674	624	100
Indomethacine	2460	1610	100
Ketoprofen	5027	3524	100
Lisinopril	253	242	100
Loratadine	14	–	25
Lorazepam	668	81	100
Mefenamic acid	335	133	100
Metoprolol	826	173	100
Metronidazole	722	617	100
Mevastatin	1008	680	100
Naproxen	2340	874	100
Nifuroxazide	1397	1215	100
Norfloxacin	66	26	100
Ofloxacin	18605	4122	100
Oxytetracycline	781	433	100
Pentobarbital	35	28	100
Phenobarbital	28	1	100
Phenylbutazone	37	19	100
Pindolol	121	100	100
Pravastatin	624	348	100
Propranolol	46	8	50
Propyphenazone	15	5	75
Ranitidine	1468	848	100
Salbutamol	62	28	100
Salicylic acid	1320	466	100
Sotalol	4751	886	100

Spiramycin	40	–	25
Sulfadiazine	32	2	100
Sulfamethazine	13	1	50
Sulfamethoxazole	4240	1570	100
Tetracycline	19	8	75
Tilmicosin	62	10	100
Trimethoprim	1192	488	100

As shown in the result table (for the complete results see table C.6) the compounds detected in major concentration are the two antibiotics Ciprofloxacin and Ofloxacin and the diuretic Furosemide. These compounds were detected in each sample with concentrations in any case major than 10 μg L^{-1}. The maximum concentration arrived till 22 μg L^{-1}.

3.6.2. Ferrara Hospital

Analytical results for Ferrara Hospital are reported in table 3.14 where the ratio $\frac{Winter}{Summer}$, the average values, the standard deviation (SD) and the frequency of occurrence with n=5 are shown.

Table C.7, instead, reports all the complete results. These tables show all the concentrations of the detected compounds, without considering the two different analytical period (september 2009 and march 2010).

Other important data reported in table 3.14, regards the ratio between winter and summer season concentrations. It is clear that in winter season the concentration of most compounds are much higher than in summer. In this hospital it is possible to examine a high variability between summer and winter.

Table 3.14.: Ferrara Hospital results (ng L^{-1}). Ratio $\frac{Winter}{Summer}$, the average values, the standard deviation (SD) and the frequency of occurrence with n=5

Compounds	$\frac{Winter}{Summer}$	**Average**	**SD**	**Frequency**
Acetaminophen	0.6	3143	1175	100
Atenolol	2.4	4409	1917	100

Atorvastatin	2.1	212	88	100
Azithromycin	16.5	497	442	100
Bezafibrate	–	199	270	60
Butalbital	11.3	226	196	100
Carbamazepine	1.0	956	195	100
Chlortetracycline	–	77	22	40
Cimetidine	–	112	133	60
Ciprofloxacin	13.1	13487	11571	100
Clarithromycin	190.8	6589	6169	100
Clenbuterol	–	1054	172	60
Clofibric acid	–	13	1	40
Codeine	3.6	1343	1234	100
Diazepam	–	31	9	60
Diclofenac	2.3	395	162	100
Doxycycline	–	76	29	40
Enalapril	2.4	239	119	100
Enoxacin	3.4	196	151	100
Erithromycin	1.9	127	63	100
Famotidine	2.5	78	40	100
Fluoxetine	1.9	45	20	100
Furosemide	0.8	6280	916	100
Gemfibrozil	–	33	28	60
Glibenclamide	1.4	85	22	100
Hydrochlorothiazide	3.2	1582	860	100
Ibuprofen	4.4	1813	1180	100
Indomethacine	0.2	1181	1258	100
Ketoprofen	1.2	1289	357	100
Lisinopril	–	213	176	40
Loratadine	–	20	6	60
Lorazepam	3.3	433	245	100
Mefenamic acid	4.7	376	278	100
Metoprolol	1.4	928	267	100

Metronidazole	2.9	704	355	100
Mevastatin	0.3	288	194	100
Naproxen	11.9	3107	4444	100
Nifuroxazide	2.3	229	102	100
Norfloxacin	10.3	222	202	100
Ofloxacin	8.5	20032	15550	100
Oxytetracycline	–	89	22	40
Paroxetine	–	67	10	60
Pentobarbital	6.7	84	61	100
Phenobarbital	12.7	157	149	100
Phenylbutazone	2.2	107	46	100
Pindolol	–	45	4	40
Pravastatin	2.4	129	86	100
Propranolol	0.5	60	27	100
Propyphenazone	–	98	–	20
Ranitidine	2.3	2338	1399	100
Roxithromycin	–	79	56	60
Salbutamol	4.5	83	53	100
Salicylic acid	2.2	1745	689	100
Sotalol	10.5	3238	2793	100
Spiramycin	–	68	37	60
Sulfadiazine	3.4	236	133	100
Sulfamethazine	–	23	9	60
Sulfamethoxazole	1.1	1921	1083	100
Tilmicosin	18.0	164	161	100
Timolol	–	33	10	60
Trimethoprim	0.3	371	317	100

Table 3.15 reports that the concentration of PhCs compounds in Ferrara Hospital have a high variation between summer and winter season. In fact the ratio between these two season ($\frac{Winter}{Summer}$) is equal to 2.8 for the average concentration and equal to 3.3 for the sum concentration. This is an expected result (although not expected

in this size) because in winter the use of antibiotics (mainly Ciprofloxacin, Clarithromycin, Ofloxacin for example) or analgesics/anti-inflammatories (like Naproxene and Salycilic acid) is really relevant, comparing with the summer use.

Table 3.15.: Ratio between winter and summer concentration in Ferrara Hospital during the experimental investigation

	Average concentration	**Sum concentration**
$\frac{Winter}{Summer}$	2.8	3.3

3.7. Discussion

Some interesting consideration about this chapter are:

- HWWs are subject to seasonal variations (see table 3.15) and in fact the experimental campaign results from summer and winter are considered separately in table 3.16.

- In terms of detected compounds, Lagosanto shows a higher value, if compared both with Ferrara summer analysis, than with Ferrara winter analysis. In particular, in Lagosanto WWs were found 59 compounds. In Ferrara WWs there were a high variability from summer (47 compounds) to winter (57 compounds).

- The more detected compounds are the two antibiotics Ciprofloxacin and Ofloxacin and the diuretic Furosemide. Moreover, in Ferrara Hospital were detected also a high concentration of the antibiotic Clarithromycin. This compound was detected in concentration lowest in Lagosanto Hospital.

- Table 3.16 shows the pro capita contribute of the PhCs. The small hospital of Lagosanto presents a really high pro capita load (expressed as ng L^{-1} $patient^{-1}$) if compared with that of Ferrara. The 5.8 ng L^{-1} $patient^{-1}$ are really a large contribute compared with the Ferrara summer values of 0.8 ng L^{-1} $patient^{-1}$. In total, referring to the reported analytical results, the sum of PhCs for patient are 305 ng L^{-1} $patient^{-1}$ in Lagosanto Hospital and *only* 38 (or 127) in Ferrara Hospital in summer (or in winter season). This is also

due to the lowest water consumption in Lagosanto Hospital (670 L bed^{-1} d^{-1}) respect Ferrara Hospital (800 L bed^{-1} d^{-1}).

- This problem puts the attention on the characteristics of the WWs, derived from a small hospital structure (Lagosanto for example) that, in terms of pollutant load, may represent an environmental problem, it is not adequately treated before the discharge in a surface water body.

  Lagosanto's WWs are collected in a public sewage and co-treated with UWWs in a CAS system (5000 i.e.). The final discharge point is an irrigational channel with a dominant flow derived from the WWTP for almost 8 month for year. Ferrara WWs are also collected in a public sewage, but co-treated with the UWWs derived from all the town (130 000 i.e.) and mixed, before the discharge in the final water body, with the industrial treated WWs derived from the nearest petrochemical site (100 000 i.e.). Then, in this case, the dilution with other kind of waters, plays a really important role in the final concentration, before the discharge. So the impact of the WWTP on the final discharge, is really low in term of PhCs concentration.

Table 3.16.: Comparison between the two studied hospital results

Compounds	**Lagosanto Summer**	**Ferrara Summer**	**Ferrara Winter**
Detected, n	59	47	57
Average, ng L^{-1}	1731	729	2055
Sum, ng L^{-1}	91591	34281	114440
Patient	300	900	900
Average pro capite, ng L^{-1} $patient^{-1}$	5.8	0.8	2.3
Sum pro capite, ng L^{-1} $patient^{-1}$	305	38	127

An interesting result of this study, is reported in table 3.17, that shows the average concentrations for the main therapeutic classes analysed. In particular, is evident that diuretic and antibiotics represent the more presents classes, derived from hospital effluents, into the public sewage.

The results shown in Sim et al. (2011) confirm that the use of antibiotics and Carbamazepine is relevant in hospital structures. The same result is found on a different study conducted during this thesis, but it is important to underline, that

Table 3.17.: Average concentration (ng L^{-1}) for the different classes in Ferrara Hospital compared with Ferrara WWTP and load percentage of the HWWs compared with UWWs

Class	**Ferrara Hospital**	**Ferrara WWTP**	**Load %**
analgesics/anti-inflammatories	1406	464	6
antibiotics	2803	311	19
antidiabetic	85	87	2
antihypertensive	885	1401	1
barbiturates	155	124	3
Beta-agonists	626	86	15
beta-blockers	1649	536	6
diuretic	6280	423	31
Lipid regulators	182	121	3
psychiatric drugs	362	225	3
Average	1443	378	9

Carbamazepine is considered an anthropogenic marker non specific for the hospital effluents, but for all kind of effluents.

CHAPTER 4

Experimental investigation

This chapter will describe the different pilot plants tested in this three years of analytical campaign. Where necessary, the structure of the thesis is maintained and a literature review comes before the experimental description.

At the beginning (section 4.1) the aim is placed on the disinfection of raw sewage, a practice not recommended in developed countries, where there are centralized WWTP. This helpful disinfection could be done in order to avoid major problems or decrease hygiene risks, where there are no WWTP in the proximity of a hospital structure.

Moreover, in section 4.2, the chapter will take in consideration Lagosanto Hospital, a new hospital with a capacity of 300 beds built 30 km far from Ferrara in 2001. The WWs derived from this hospital were studied with two different biological pilot plant. These two MBR pilot plants present two different kind of membrane (MF - UF) and analysis about BOD_5, COD, SS and other macropollutants were done. The data regarding the PhCs in this effluents were reported in chapter 3 in particular in section 3.6.1, because the experimental investigations with the two tested pilot plants described in this chapter were only about the macropollutants and they did not regard PhCs compounds.

In another part of the study, the experimental investigation was about the WWs

deriving from the WWTP of La Spezia (section 4.3), where an MBR pilot plant is tested and compared with the La Spezia CAS system.

At paragraph 4.4 PhCs were studied in inlet and outlet of Ferrara WWTP, in order to analyse the removal rate of a conventional system. This WWTP treat a mix of urban and hospital (low percentage) WWs.

Paragraph 4.5 is about the polishing treatment obtained after the conventional WWTP in Ferrara with a natural treatment, like a constructed wetland (CW) pilot plant, working as tertiary system. The aim of this section was understand the buffering capacity of the natural treatment.

In order to confirm the buffering step of a final natural polishing treatment, another experimental investigation was developed in section 4.6. The final effluent of the Ferrara WWTP was drugged with three PhCs and the influent and effluent concentration in CW were analysed. Aim of this experimental investigation was understand the efficiency of the natural step with high pharmaceuticals concentration.

All these steps are tested because, with the literature data, it is possible to say that a MBR system can remove a lot of PhCs but a polishing final treatment is recommended mainly to treat particular effluent like HWWs.

An approach to this problem that consider the different PhCs as recalcitrant compounds and that take in consideration the difficult in removing from the liquid phase these pollutants is recommended and a multibarrier system is the best technology to adopt. For more details about the different technologies (see chapter 5).

4.1. Disinfection of raw HWWs

This section will talk about the raw WWs disinfection with peracetic acid (PAA) or with hypochlorite and it does not speak direct about the removing of PhCs from the water. In addition to the different MBR, CAS or CW systems tested, also a disinfection process could presents a real importance in the management and treatment of HWWs mainly for the reduction of health risk.

This treatment sequence can provide a rapid solution of treatment in those cases in which hospital effluents are commonly not treated at all and are directly discharged into a surface water body. As this practice is absolutely to avoid, in order to pre-

vent the spread of pathogens microorganisms in water cycle, the tested sequence of treatment, represents a strategy for the hospital effluent management, waiting for planning actions, including the construction of more complete WWTPs where not only hospital, but also urban, industrial WWs could be conveyed and adequately treated before their immission in surface bodies.

Disinfection is a treatment aimed at significantly reducing the content of microorganisms (bacteria, viruses, protozoa) in WWs to a level of safety suitable for the final use of the treated effluent (discharge into a surface water body or reuse). Microorganism abatement or inactivation, may be performed by various mechanisms: chemical (reactions with added agents) physical (radiation absorption, membrane retention) or natural (natural death), solar radiation, high temperature, competition and predation). Microorganisms may be definitively removed or separated into another phase (liquid or solid).

Assuming that the microorganism concentration in the influent and effluent of the disinfection stage is respectively N_0 and N, the microorganism inactivation rate may be expressed as percentage removal rate η, given by Eq. 4.1:

$$\eta = \frac{N_0 - N}{N_0} \times 100 \tag{4.1}$$

or as log reduction that is log units (l.u.), given by Eq. 4.2:

$$l.u. = \log \frac{N_0}{N} \tag{4.2}$$

The correlation between l.u. and η is given by Eq. 4.3:

$$l.u. = -\log\left(1 - \frac{\eta}{100}\right) \tag{4.3}$$

Reduction of bacterial content in the WWTP depends on the effectiveness of each single stage (ATV (1998), Metcalfe and Eddy (1991)). Viruses are reduced by a factor of some 2 powers of ten, through adsorption onto sludge. Worm parasites and/or their adult stages, are increased by 70% to 90 % in the sludge of the mechanical phase. However, partial reactivation of all these microorganisms may occur, especially in case of ultraviolet (UV) disinfection.

Conventional disinfection is a treatment aimed at reducing bacterial load, generally faecal coliform (FC), to a level of 500-1000 MPN/100 mL[1] in the final effluent, prior to either its discharge into a surface water body (sea, lake or river) or its reuse. In the case of direct reuse in the absence of particular restrictions, or for GW recharge, on the other hand, advanced disinfection may be necessary to further reduce the microbial load (faecal or total coliforms) to 2-100 MPN/100 mL.

Conventional disinfection involves a removal rate of 2-3 l.u., which is easily guaranteed by modest concentrations of disinfectants and contact times. For instance, if secondary biological effluents with an FC concentration of 10^5 MPN/100 mL are subjected to conventional disinfection which reduces its bacterial content by 2 l.u., the final concentration will be equal to 10^3 MPN/100 mL, an acceptable level for various effluent purposes. In contrast, advanced disinfection requires higher concentrations and longer contact times, and therefore results in higher doses (= concentration x contact time).

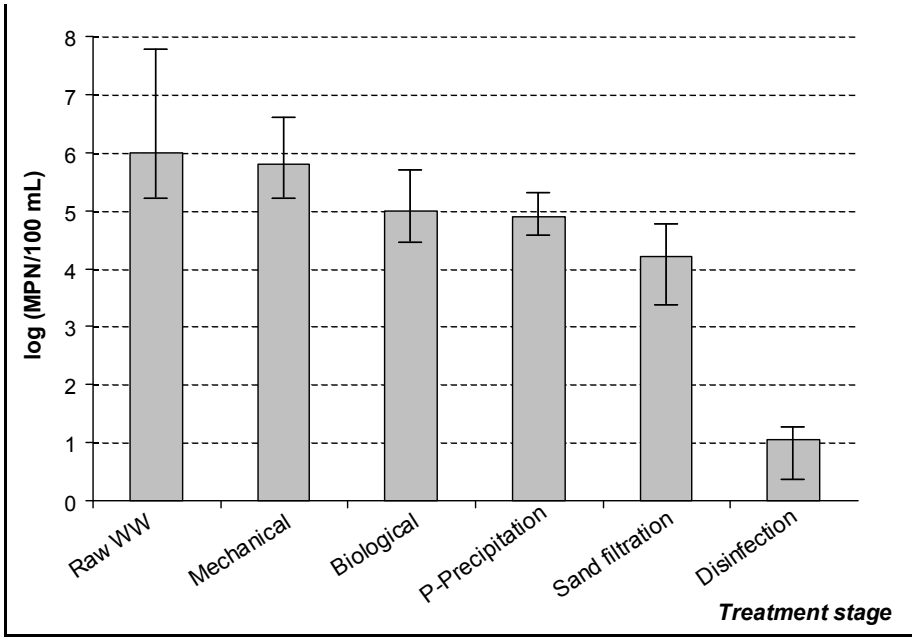


Figure 4.1.: FC levels in raw WWs and in the effluents of different treatment steps in a municipal WWTP

Direct chlorination or primary treatment followed by chlorination is the most widely used method for disinfecting HWWs in order to prevent the spread of pathogenic

[1]The concentration of bacteria is generally reported as MPN/100 mL or CFU/100 mL, respectively the Most Probable Number and the number of Colony-forming Units per 100 mL, depending on the method used for their estimation in a water sample.

microorganisms, causal agents of nosocomial infectious diseases (Liu et al. (2010)).

The widespread medical use of chlorine disinfection is due to its very broad spectrum of biocide activity against bacteria, virus and fungi and simple operation. However, this method is capable of producing undesirable disinfection by-products (DBPs), its efficacy depends much upon the quality of the feed water and in particular low efficiency of virus removal.

4.1.1. The experimental campaign

The management and the treatment of HWWs are an interesting field of research and discussion for scientists, hygienists, environmental engineers, economists and administrators. They depend on different factors: legal requirements, existing WWTPs, environmental conditions and accuracy. The discharge without any kind of treatments is absolutely to avoid, a treatment is always necessary, a basic or advanced one has to be adopted in the different situations. Pollutants concentration must be reduced.

The best sequence of treatment should be defined on the basis of the hospital characteristics (mainly size and wards), the receiving water body (average flow rate, autodepurative capacity, final use), the environment conditions (temperature, urban context...), the existing WWTPs near the hospital to which the effluent can be conveyed.

The basic treatment to adopt for HWWs is the main objective of this research. A sequence of preliminary treatments (mechanical ones) and a chemical disinfection is investigated in order to evaluate the bacteria removal from a hospital effluent. NaClO and CH_3COOOH (peracetic acid, PAA) have been tested at different concentrations and contact times on the raw effluent from a small hospital, in Italy. The scheme of the pilot plant (10 m^3 h^{-1}) tested in this investigation is reported in figure 4.2.

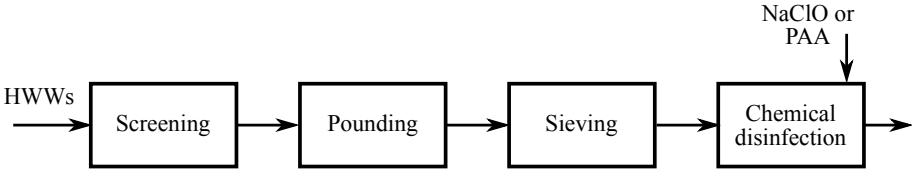


Figure 4.2.: Scheme of the pilot plant for disinfection experimentation

Table 4.1.: Characteristics of HWWs, UWWs and Italian legal limits for discharge

Parameter	**HWWs**	**UWWs**	**Legal limits**
SS, mg L^{-1}	10-1400	30-300	80
BOD_5 , mg L^{-1}	100-1600	10-130	40
COD, mg L^{-1}	280-9000	90-500	160
COD/BOD_5	1.4-6.6	1.7-2.4	
Total P, mg L^{-1}	3-8	8	10
N-NH_3, mg L^{-1}	10-55	30-40	15
Chlorides, mg L^{-1}	80-188	50	1200
Hg, μg L	0.04-0.28	< 0.5	5
Total surfactants, mg L^{-1}	3-7.22	4-8	2
Total Coliform, MPN/100 mL	10^6-10^9	10^7-10^8	
Fecal Coliform, MPN/100 mL	10^3-10^7	10^6-10^7	
E. coli, MPN/100 mL	10^3- 0^7	10^6-10^7	$5{\cdot}10^3$

For the experimental investigation the used WWs derived from the effluent of a small hospital (50 beds) located near Rimini, Northern Italy.

The observation period were of two month in October-November 2009 and the analysed compounds during this period were Total Coliform (TC), *E. coli* and Suspended solids (SS).

The adopted analytical methods were the standard reported in APHA (2001).

Table 4.2.: Applied concentration and contact time for the two disinfectant during the experimental investigation

Disinfectant	**Applied concent. mg L^{-1}**	**Contact time min**	**Number of samples analyzed**
NaClO	5, 10, 15, 20	10, 20, 30	24
PAA	5, 10, 15, 20, 40	10, 20, 30	36

Table 4.3 reports the state of the art about the predisinfection of raw WWs. All the literature data reported derived from: Carrasco and Turner (2006), Sanchez-Ruiz et al. (1995), Kitis (2004), Koivunen and Heinonen-Tanski (2005), Falsanisi et al. (2006), Wiley (1999).

4.1.2. Results

On the basis of this experimental campaign it is possible to conclude that:

- PAA is able to reach higher removal rate for TC than *E. coli* (0.5-1 log unit

Table 4.3.: State of the art - Predisinfection of raw WWs

Disinfectant	Authors	PAA, mg/L	t_{cont}, min	c x t mg min/L	TC removal (log unit)	*E. coli* removal (log unit)
PAA	Sanchez Ruiz *et al.,* 1995 (Initial TC 10^6-10^8 MPN/100 mL)	2	15	30	0.95	
		10	15	150	0.84-2.5	
		15	15	225	3.75	
		20	15	300	3.45-6.45	
		30	15	450	0.8-5.7	
		80	15	1200	2	
	Kitis, 2004 (Initial TC 10^4-10^8 MPN/100 mL)			40	1	0.6-2.5
				150	0.7-3	3.7
				225	3.7	0.75
				300	3.6	
	Koivunen et al., 2005 (Initial TC 10^6-10^8 MPN/100 mL)	5	4-10	20-50	0.4-0.6	
		10	4-10	40-100	2.2-3.2	
		15	4-10	60-150	3.4-3.7	
		5	10-20	50-100	0.7-0.9	
		10	10-20	100-200	3.4	
		15	10-20	150-300	3.9	
		5	20-30	100-150	1	
		10	20-30	200-300	3.5-3.6	
		15	20-30	300-450	3.8-3.9	
	Carrasco and Turner, 2006 (Initial TC 10^7 MPN/100 mL) (Initial *E. coli* 10^6-10^7 MPN/100 mL)	2	15	30	0.56	0.57
		2	30	60	0.48	0.48
		10	15	150	0.46	0.29
		5	30	150	0.43	0.30
		15	20	300	0.37	1.1
		15	30	450	0.75	0.84
		15	40	600	2.57	3
		30	40	1200	2.91	2.7
	Falsanisi et al., 2006 (Initial TC 10^6 MPN/100 mL) (Initial *E. coli* 10^5 MPN/100 mL)	30-40	5	~175	2.94	4.55
			10	~ 350	3.15	4.74
			20	~ 700	3.40	4.93
			40	~1400	3.97	5.11
NaClO	Geo. Clifford White, 1999 (Initial TC 10^6-10^8 MPN/100 mL)	12-40	15-30	180-1200	3-4	
	Carrasco and Turner, 2006 (Initial TC 10^7 MPN/100 mL) (Initial *E. coli* 10^6-10^7 MPN/100 mL)	4	15	60	0.42	0.33
		6	15	90	0.54	0.33
		4	30	120	0.27	0.27
		10	15	150	3.27	
		20	15	300	3.27	
		30	15	450	3.27	
		40	15	600	3.97	
		50	15	750	4	

of difference on average at the same applied dose c x t) (Figure 4.3).

- On the contrary, NaClO is a bit more effective with *E. coli* than TC (Figure 4.4).

- Experimental data are quite spread due to the different characteristics of the raw WW, influent to the pilot plant, in particular suspended solids that varied in a wide range (Table 4.4). About this table some considerations are that according to literature data, a concentration of SS up to 100 mg L^{-1} does not influence the biocidal action of PAA. Greater concentrations can reduce it.

Table 4.4.: SS, *E. coli*, TC in the influent to the pilot plant

SS	**Experimental data**
Sample number	10
min, mg L^{-1}	133
max, mg L^{-1}	1426
Average, mg L^{-1}	504
S.D., mg L^{-1}	484
E. coli, MPN/100 mL	10^5-10^7
TC, MPN/100 mL	10^7

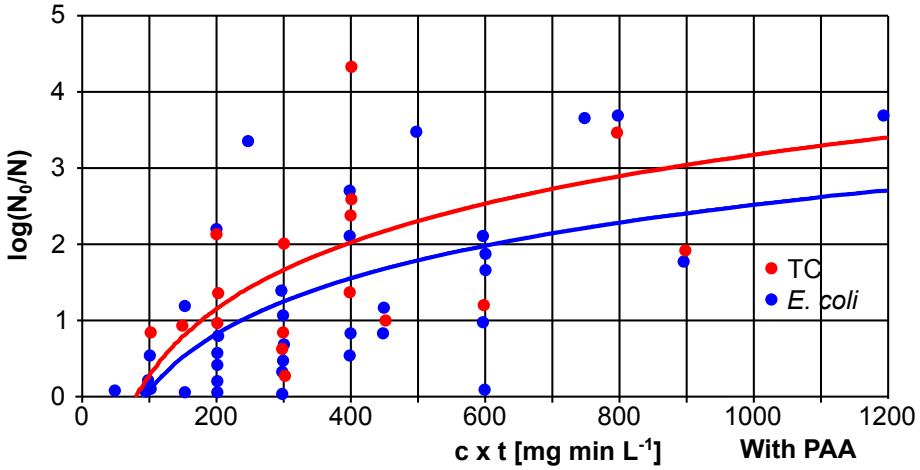


Figure 4.3.: TC and *E. coli* removal with PAA (experimental data)

On the basis of few literature data: *E. coli* is better removed with PAA and TC with NaClO (Figure 4.5 and Figure 4.6).

With a raw WW of these characteristics (with a high SS content), at least:

- 600 mg min L^{-1} of PAA or

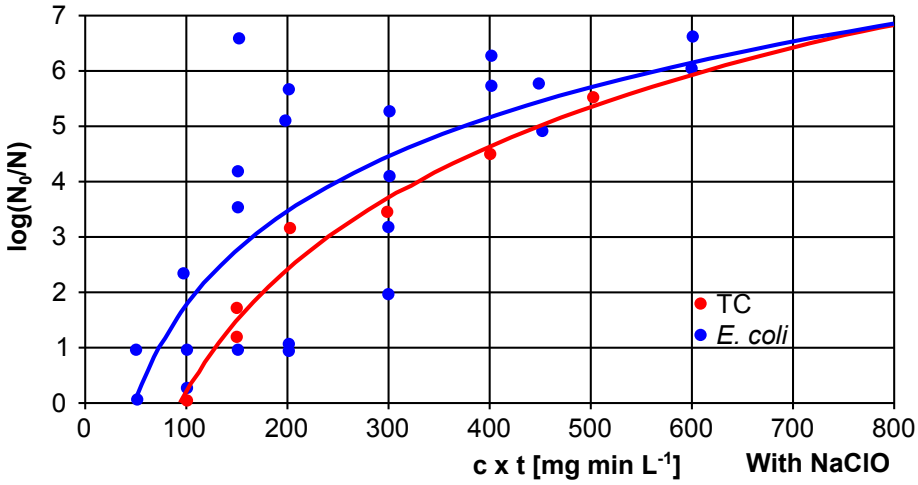


Figure 4.4.: TC and *E. coli* removal with NaClO (experimental data)

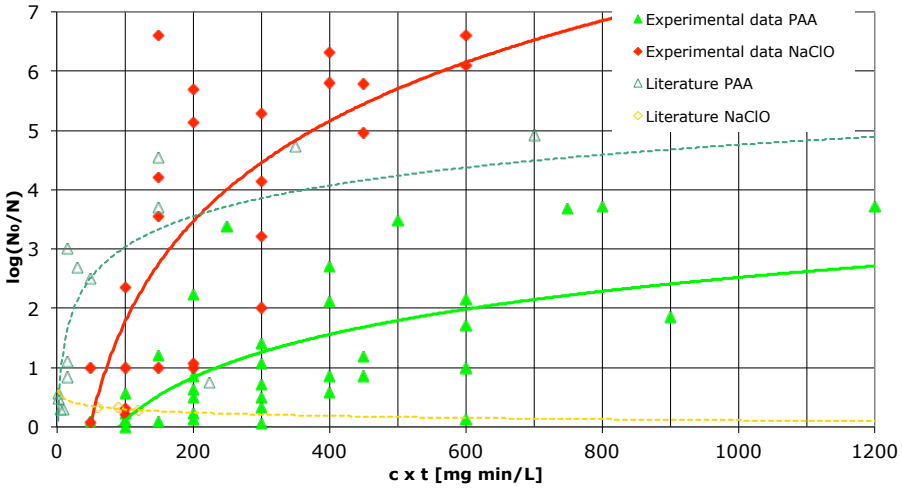


Figure 4.5.: *E. coli* removal with PAA and NaClO

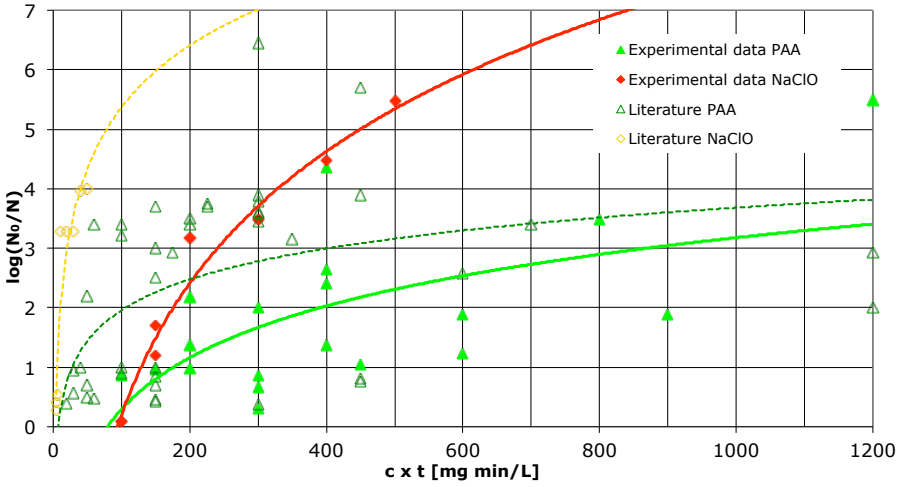


Figure 4.6.: TC removal with PAA and NaClO

- 150 mg min L^{-1} of NaClO

are required to reach a reduction of 2 log units of *E. coli* and at least:

- 400 mg min L^{-1} of PAA or
- 200 mg min L^{-1} of NaClO

to reach a reduction of 2 log units of TC.

Further researches are necessary in order to investigate the disinfection action of PAA and NaClO at a lesser content of SS in raw WWs. Hence it is really important to guarantee an efficient pretreatment step including a degritting, a pounding, a sieving and a sedimentation in order to separate solids of different size that may be present in the (hospital) effluent and could reduce the disinfection effect.

4.2. MBR pilot plants in Lagosanto

This section will describe the experimental investigations about two different MBR pilot plants treating the hospital effluent derived from Lagosanto Hospital. For basic information about MBR literature data see paragraph 5.1.3.

4.2.1. Screening of HWWs

As already reported the Lagosanto Hospital (built 30 km far from the town of Ferrara) is a structure in operation since 2001 with a capacity of 300 beds.It presents the different departments of surgery, orthopedics, traumatology, obstetrics and gynecology, pediatrics, gastroenterology, cardiology, urology and psychiatry.

All the producted WWs (toilets, kitchen, pharmacy and the internal laundry) are collected from the internal sewage, that consists in a separate type (stormwaters are collected separately), and conveyed in 47 Imhoff tank (with an average of about 20 i.e. each) and, after a mild disinfection with sodium hypochlorite, are released into the public sewer and conveyed in the local WWTP that also receives the UWWs derived from the near town of Lagosanto. The HWWs accounts for 16% of the total flow treated at the WWTP in dry weather.

The experimental investigation was in support of the design choices for the construction of the new WWTP for the new Ferrara Hospital, a 900 beds hospital under construction 5 km far from Ferrara.

For this reason the experimental studies were conducted with a real effluent deriving from the Lagosanto Hospital with the aim of:

1. understand the qualitative and quantitative nature of the HWWS before placing it into the public sewer in order to identify the most representative pollutants

2. testing different pilot plants in order to evaluate the removal efficiency of biological treatments comparing the removal rate with flat panels (MF), hollow fiber (UF) and conventional systems

This part of the study was conducted between May 2007 and March 2008, focused on the qualitative and quantitative aspect of the macro and micro parameter. An in-depth survey conducted in collaboration with the local sanitary company, has identified the types of drugs most commonly used at the hospital on an annual basis. Antibiotics, anti-inflammatories and cortisone are the products most administered. To these products we must add the antiepileptic drug carbamazepine.

The average monthly consumption shows significant changes, as described in figure 4.16 at page 114 and 4.17 at page 115.

For the qualitative and quantitative characterization of the raw HWWs (before chlorination), we decided to limit the investigation to the antibiotics and carbamazepine and the full list of analyzed compounds in this phase of the study is reported in table 4.5.

The research of these micropollutants has been extended to the inlet and outlet WWs from Lagosanto WWTP, in order to compare the contribution of the urban and hospital WWs and to evaluate the removal rate with conventional treatment systems (activated sludge).

The analysis of PhCs were made using LC-ESI-MS/MS with 24 hours composite samples collected in 1 liter plastic bottles taken during three different day on July 9, 10, 11, 2007. Each sample was taken in no rain day, in order to avoid a possible dilution.

In this particular month, the average consumption of antibiotics and carbamazepine in the hospital structure, is major than the average monthly consumption. All the analysis done in this period showed that, for all the investigated parameter, only Cefazoline and Carbamazepine was above the detection limits.

Moreover, the concentration of Cefazoline and Carbamazepine at the inlet of the Lagosanto WWTP, was higher than in the HWWs, probably due to a major load of these substance from UWWs.

Table 4.5.: Antibiotics and Carbamazepine in Lagosanto HWWs, influent and effluent of Lagosanto WWTP

Parameter, μg L^{-1}	**Hospital**	**WWTP influent**	**WWTP effluent**
Amoxicillin	–	–	–
Ampicillin	–	–	–
Cefamandole	–	–	–
Cefoperazone	–	–	–
Denofloxacin	–	–	–
Dicloxacin	–	–	–
Enrofloxacin	–	–	–
Flumequine,	–	–	–
Oleandomycin	–	–	–
Penicillin	–	–	–
Spyramicin	–	–	–
Sulphadiazine	–	–	–
Sulphadimidine	–	–	–
Sulphaguadinine	–	–	–
Sulphamerazine	–	–	–
Sulphametoxypiridazine	–	–	–
Sulphathiazole	–	–	–
Tylosin tartrate	–	–	–
Cefazoline	0.23	3.57	–
Carbamazepine	0.54	1.05	0.44

The low values reported in table 4.5, probably are due to an uncorrect conservation of the samples, that cause a rapid degradation of the detected compounds.

The aim of the experimental investigation was evaluate the tractability of the HWWs using biological systems. For this reason two different MBR pilot plants were tested:

- in the first part of the experimental investigation (from July to October 2007) the pilot was a MBR Kubota plane membrane (MF) with a pore diameter of 0.45 μm (see figure 4.7)

- in the second part of the investigation (from October to March 2008) the pilot was an MBR hallow fiber membrane (Puron UF) with a pore diameter of 0.01 μm (see figure 4.8)

(a) Kubota pilot plant

(b) Plane membrane

Figure 4.7.: The first membrane pilot plant tested (Kubota membrane)

(a) Puron pilot plant

(b) Hallow fiber membrane

Figure 4.8.: The second membrane pilot plant tested (Puron membrane)

The main characteristics of the two pilot plants are reported in table 4.6. In each phase the HWWs, taken with a pump from the final well before the chlorination, was added continuously in the biological reactor.

Aeration was made by air insufflation from the bottom of the nitrification compartment and in the second pilot, larger than the first one, the dissolution of the mixture of water and oxygen was guaranteed by the movement of an agitator. The permeate extract was drained into a second well to prevent interference with the feed plant.

Table 4.6.: Characteristics of the two MBR pilot plants studied in Lagosanto

Parameter	**MF**	**UF**
Period	July-October 2007	October-March 2008
Membrane	Plane	Hallow fiber
Pore diameter, μm	0.45	0.01
Superf. flux, L $m^{-2}h^{-1}$	11	15-35
Flow rate, L h^{-1}	4	90
Volume, m^3	Denitr. 0.2 - Nitr. 0.5	Nitr. 1.5
TMP pressure, mbar	200-250	400
Tot. surf. membr., m^2	0.37	5
HRT, d	6	0.6
Sludge age, d	40	40
Membrane cleaning	1. Air insufflation 2. Chemical cleaning	1. Air insufflation 2. Relaxation 3. Backwash with permeate 4. Chemical cleaning

In the second phase of the experimental investigation, another aim was to compare the CAS process efficiency with the MBR system under studying. To do this we did not built another plant, but we used the same installed pilot using it as MBR or SBR (Sequencing Batch Reactor) in function of the requirement. When we tested SBR sequence we used the aeration tank (without the air insufflation) like a sedimentation basin with a retention time of 2-3 hours.

During the starting period, each pilot is filled with an inoculum of activated sludge taken from the Lagosanto WWTP. After a period of start up of about 30 days, it was possible to start the analytical planning and the experimental investigation. The conventional macroparameter analysed in this part of the investigation were: BOD_5, COD, filtered COD (with a 0.45 μm membrane), SS, P_{Tot}, NH_4, anionic, cationic, non ionic and total surfactants, Hg, *E. coli*, Cefazoline and Carbamazepine.

The influent and effluent samples from the pilot and from Lagosanto WWTP were made instantly, on the same day during the week. In particular, during the second investigation phase, permeate (effluent of the MBR) and clarified (effluent of the SBR) were obtained respectively at about 8 am and at 11, this was made to evaluate the characteristics of the WWs maintaining equal environmental conditions.

The samples were immediately transported to the laboratory thermostated and analysis on conventional macroparameter were made. In this first phase of the exper-

imental investigation, the analysis of micropollutants were done in to a specialized and certified laboratory.

The sampling points (reported in figure 4.9) were as follows:

1. HWWs before chlorination,
2. Permeate (extracted through the membranes)
3. Clarified (after sedimentation of 2-3 hours to simulate an activated sludge process),
4. Influent Lagosanto WWTP,
5. Effluent Lagosanto WWTP

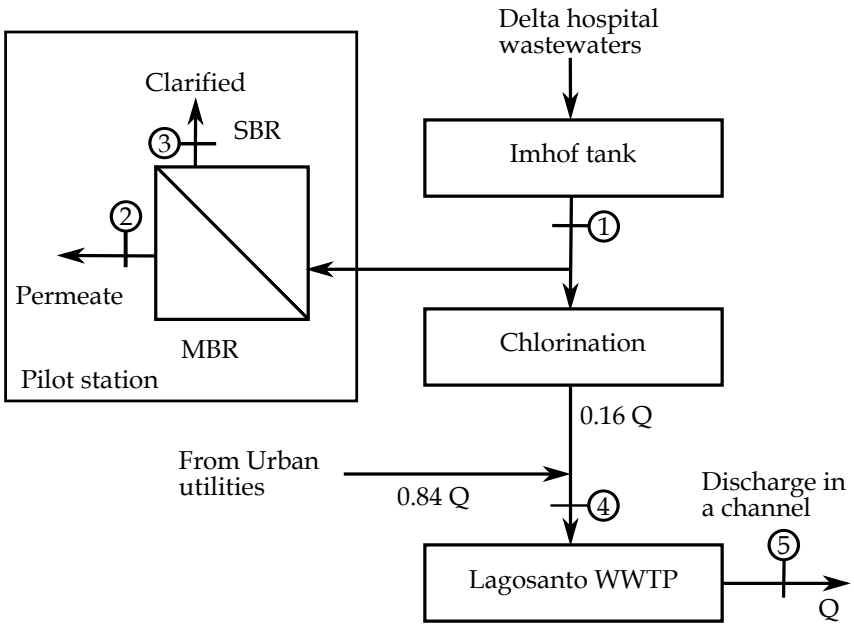


Figure 4.9.: Sampling point and pilot scheme

An in-depth literature review completed this part of our investigation. Data were collected for BOD_5, COD and SS in effluents of hospitals of different sizes, services (60-900 beds) and countries (Italy, France, Turkey, India, Iran, Thailand, Canada and Greece) (Nardi et al. (1995), Wangsaatmaja (1997), Emmanuel et al. (2001), Brown et al. (2006), Tsakona et al. (2007)Kummerer et al. (1997), Laber et al. (1999), Altin et al. (2003), Chiang et al. (2003), Emmanuel (2004), Wen et al. (2004), Mohee (2005), Rezaee et al. (2005), Kajitvichyanukul and Suntronvipart (2006), Pauwels

and Verstraete (2006), Gautam et al. (2007), Machado et al. (2007), Sarafraz et al. (2007), Boillot et al. (2008), Suarez et al. (2009)). Minimum and maximum values for each of the three parameters in HWWs were grouped and elaborated in order to obtain their corresponding cumulative frequency curves for each of the three parameters, giving both the minimum and maximum cumulative frequency curve. These curves are reported in Figures 4.10, 4.11 and 4.12 where they define the grey bands representing the expected variability range for each of the three monitored parameter in HWWs. Each curve is based on 25-30 literature values.

Concentrations of BOD_5, COD, SS in the Lagosanto WWs was also analyzed weekly during the experimental investigations period. These experimental curves were compared with those drawn on the basis of literature data related to the minimum, average and maximum BOD_5, COD and SS concentrations of HWWs. So these figures are the same showed in figures 3.6, 3.7, 3.8, but in this case the literature data are completed with experimental results obtained in the analytical campaign. Generally, all the data referred to the whole hospital effluents, in some cases to specific departments, such as dialysis, pediatrics, infectious and tropical diseases.

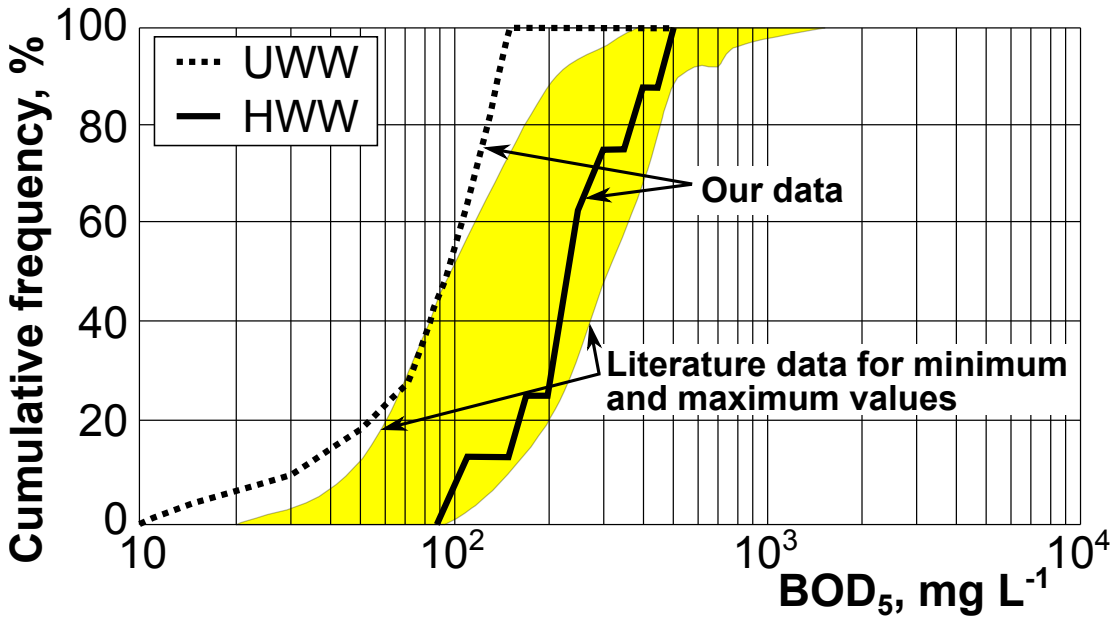


Figure 4.10.: BOD_5 cumulative frequency curves for the effluent of Lagosanto Hospital (HWWs) and the influent to Lagosanto WWTP (UWWs) and variability range for HWWs according to literature data

As reported for each of the three parameters, the concentrations in HWWs deriv-

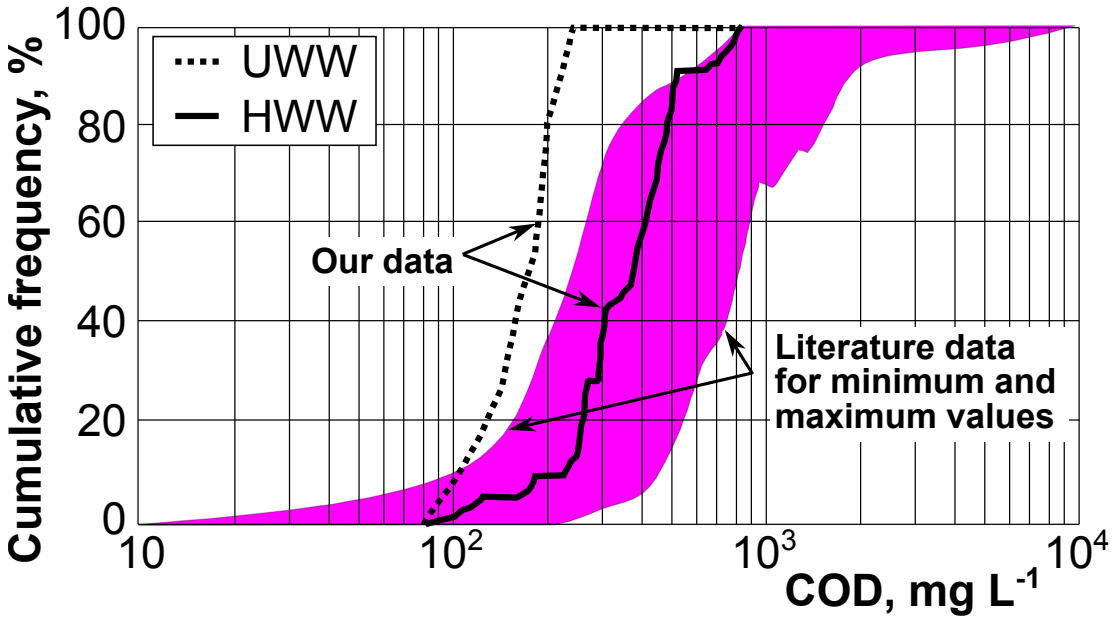


Figure 4.11.: COD cumulative frequency curves for the effluent of Lagosanto Hospital (HWWs) and the influent to Lagosanto WWTP (UWWs) and variability range for HWWs according to literature data

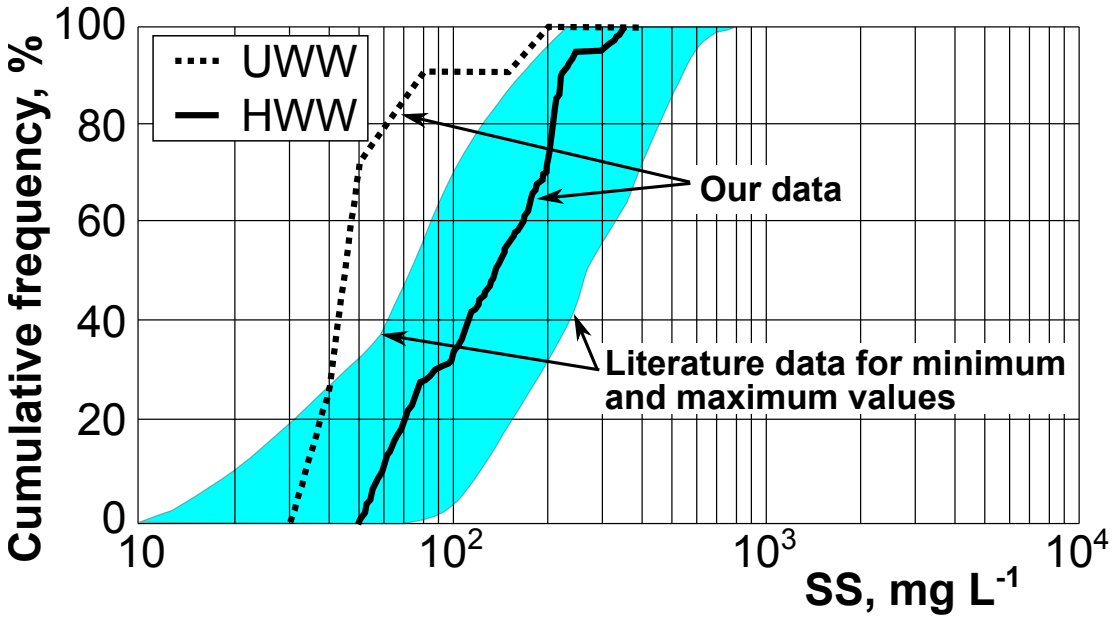


Figure 4.12.: SS cumulative frequency curves for the effluent of Lagosanto Hospital (HWWs) and the influent to Lagosanto WWTP (UWWs) and variability range for HWWs according to literature data

ing from this experimental campaign are in line with literature data and always on top of the urban line, confirming the major pollution load discharge for the three macroparameter in HWWs as jet reported in table 3.4.

Figures 4.13 and 4.14 show the changes in concentration of COD and SS in the HWWs during the day and the trend found by Emmanuel (2004) in the effluent of a department of infectious and tropical diseases. The maximum COD concentration values was both in Emmanuel (2004) research than in our studies at 18:00.

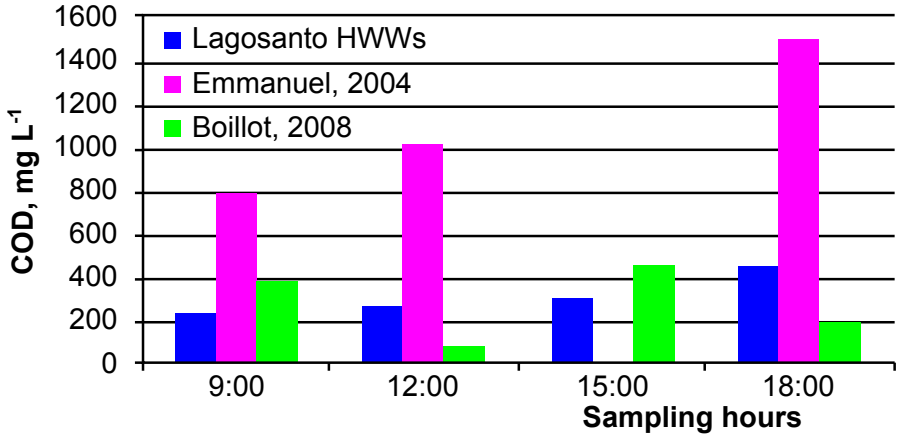


Figure 4.13.: COD variation in Lagosanto effluent. Comparison with Emmanuel (2004) and Boillot et al. (2008)

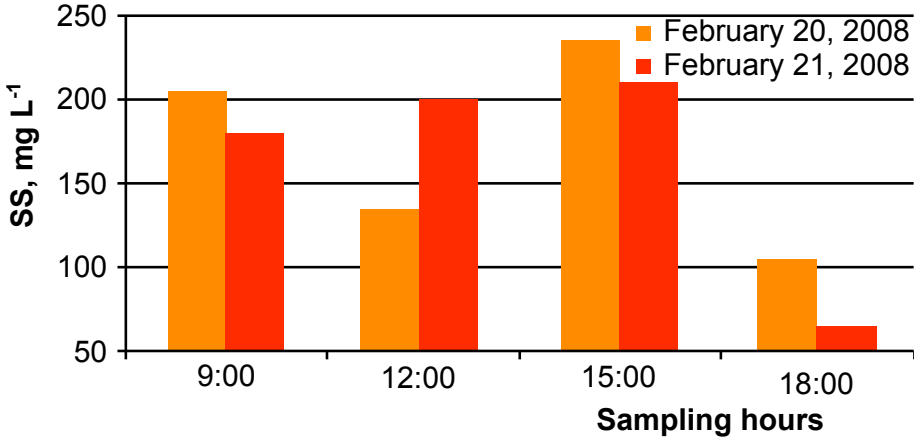


Figure 4.14.: SS variation in Lagosanto effluent during the day

Moreover figure 4.15 reports the results deriving from the analytical campaign hours by hours for COD and for SS.

The ratio between COD and BOD_5 in HWWs is usually considered in the range of 2-2.4, in agreement with the values found in Altin et al. (2003) and confirming the applicability of the correlation of their proposal, made on the data of 5 Turkish

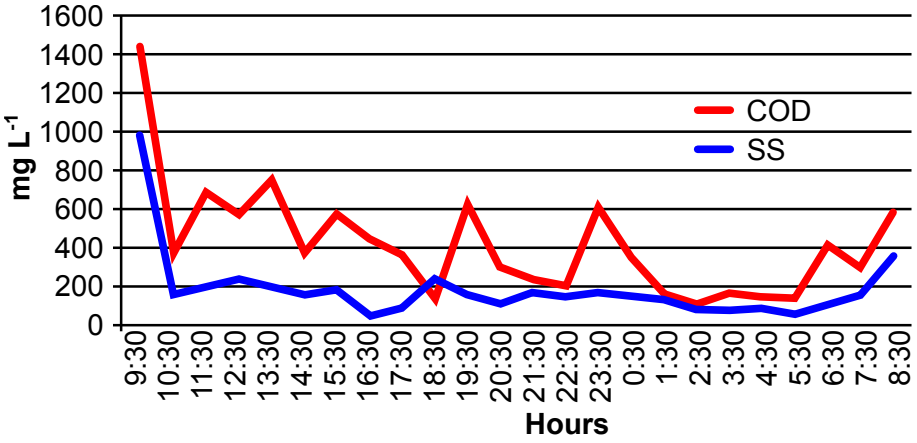


Figure 4.15.: COD and SS variation in Lagosanto effluent hours by hours in a day during the experimental investigation

hospitals of various sizes as reported in equation 4.4:

$$\ln(COD) = 1.16 \cdot \ln(BOD_5) - 0.069 \tag{4.4}$$

Literature data show that for particular departments, the ratio may be significantly different: Chiang et al. (2003) found a value of 6.6 for the effluent from a dialysis unit.

Comparing the analysis about micropollutants (only referring to the two detected compound: Cefazoline and Carbamazepine) we found concentrations major in UWWs than in HWWs. This can be explained because in hospital, water consumption per patient, is 2-3 times higher than in urban utilities. In fact making a *virtual* assessment consumption per inhabitant (table 4.7) the daily contribution pro capita are comparable.

Table 4.7.: Carbamazepine (CBZ) *virtual* consumption pro capita during the experimental investigation

Users	**i.e.**	**Specific flow** $\mathbf{L\ i.e.^{-1}\ d^{-1}}$	**Flow** $\mathbf{m^3 d^{-1}}$	**CBZ** $\mathbf{\mu g\ L^{-1}}$	**CBZ** $\mathbf{mg\ d^{-1}}$	**CBZ** $\mathbf{mg\ i.e.^{-1} d^{-1}}$
Hospital	300	600	180	0.54	97.2	0.324
Urban	4000	300	1200	1.05	1260	0.315

On the basis of the conducted experimental investigation on the Lagosatnto Hospital effluent and on the influent of the Lagosanto WWTP, we found significant differences between the two kinds of effluents. These results are reported in table

4.8. UWWs results from a greater number of samples because they include historical data sets where available.

Table 4.8.: Number of samples and range of variability for HWWs and UWWs

Parameter	HWWs		UWWs	
	Samples	Average	Samples	Average
BOD_5, mg L^{-1}	20	240 ± 82	130	70 ± 43
COD, mg L^{-1}	20	480 ± 125	130	180 ± 74
$COD_{filtered}$, mg L^{-1}	20	331 ± 54	20	118 ± 36
SS, mg L^{-1}	20	227 ± 57	130	41 ± 15
NH_4, mg L^{-1}	20	42 ± 9	130	25 ± 7
Total P, mg L^{-1}	20	6 ± 2	130	3 ± 1
E. coli, CFU/100 mL	20	$2{\cdot}10^5$ - $2{\cdot}10^6$	130	$8{\cdot}10^5$ - $4{\cdot}10^6$

Referring to hospital water consumption, our experimental investigation revealed that the specific rate per patient is about 600-700 L patient^{-1} d^{-1}.

As to faecal bacteria, we limited our investigation to *E. coli* and we found similar concentrations in the monitored hospital and urban WWs. This result is in agreement with other authors, among them: Nardi et al. (1995), Leprat (1998); Emmanuel (2004), Wen et al. (2004), Boillot et al. (2008); Sun et al. (2008).

In order to complete the comparison between the two effluents, it is important to underline that the main differences could refer to the presence of multiple drug-resistant (MDR) bacteria. Few studies are available on this topic. Chitnis et al. (2000) found that MDR bacteria population in Indian hospitals ranges from 0.58 to 40%, while it is less than 0.00002 to 0.025% in UWWs. This means that adequate treatments for hospital effluents are required in order to avoid the spread of such bacteria to the environment and in particular to the community, and it is important to verify the disinfection efficiency of the adopted treatment sequence.

Halling-Sorensen et al. (1998), Davidson (1999), Schwartz et al. (2002), Emmanuel et al. (2005b) found and investigated the main factors that contribute to the development and spread of resistance:

- mutation in common genes that extend their spectrum of resistance
- transfer of resistance genes among diverse microorganisms
- increase in selective pressures that enhance the development of resistant organisms

Markers of viral pollution in water, such as enterovirus, adenovirus, rotavirus, parvovirus, reovirus, Norwalk virus, calcivirus and coronavirus, have been identified in the hospital effluents (Leprat (1998)).

Regarding the consumption of PhCs, we made an investigation in collaboration with the in-house pharmacy service of the Lagosanto Hospital, and we found that on an annual basis, the classes of substances most commonly administered are analgesics and antibiotics, followed by cytostatics, anesthetics and contrast media.

On the basis of an in-depth literature review, we found the concentration ranges for the main groups of PhCs in HWWs as well as in UWWs (table 4.9).

Table 4.9.: Concentration range of PhCs in HWWs and UWWs. Literature data

Class	**Examples**	**HWWs (μg/L)**	**UWWs (μg/L)**
Analgesics	Diclofenac, ibuprofen, ketoprofen, paracetamol, salycilic acid	0.07-1368[a]	0.01-483[e]
Antibiotics	Ciprofloxacin, erythromycin, tetracycline	0.04-125[b]	0.01-31.70[f]
Cytostatics	5-fluorouracil, ifosfamide	0.001-124[c]	0.01-7[g]
Contrast media	Iopromide, iopamidol	0.2-2500[d]	0.2-22h
Hormones	17β-estradiol, estriol, estrone	0.017-0.2[a]	0.001-0.2[i]
β-blockers	Atenolol, metroprolol, propranolol	0.4-25[a]	0.01-15[e]

[a]Thomas et al. (2007); [b]Duong et al. (2008); [c]Mahnik et al. (2007); [d]Weissbrodt et al. (2008); [e]Kasprzyk-Hordern et al. (2008); [f]Radjenovic et al. (2009); [g]Kummerer et al. (1997); [h]Ternes and Joss (2006); [i]Teske and Arnold (2008).

Concentrations in HWWs are generally 2-100 times higher than those in UWWs, but some PhCs, like hormones and β-blockers, are present at the same levels both in urban and hospital effluents, due to their prolonged and diffuse individual consumption.

PhCs are generally persistent compounds, able to resist normal WWs treatments. Their treatability characteristics, mainly biodegradability, adsorption or absorption

tendency, and half-life time, may be significant different even among substances of the same therapeutic class (Jones et al. (2005a); Oppenheimer et al. (2007); Suarez et al. (2008); Radjenovic et al. (2009)).

4.2.2. Water consumption in Lagosanto Hospital

The study shows that water consumption in Lagosanto Hospital was about 600-700 L $bed^{-1}d^{-1}$ and in other hospitals in Ferrara area vary between 700 and 800 L $bed^{-1}d^{-1}$.

The literature data referring to hospitals in different countries (table 4.10) indicate a variability range between 340 and 1182 L $bed^{-1}d^{-1}$. Comparing hospital consumption (L $bed^{-1}d^{-1}$) with their potential (beds) were not found any significant correlation.

Finally, literature data show that the change in consumption during the day varies between +20% and -30% as for example reported in Joss et al. (2005). During the year, the largest consumption are meet in the summer months.

Table 4.10.: Water consumption in hospital structures

Source	**Consumption L $bed^{-1}d^{-1}$**	**Country**
Lagosanto	670	Italy
Ferrara's zone	700-800	Italy
Emmanuel (2004)	750	France
Emmanuel (2004)	970	USA
UBC, Technical Guidelines 2008	680	USA
Sarafraz et al. (2007)	362	Iran
Metcalfe and Eddy (1991)	738	USA
Wangsaatmaja (1997)	1182	Thailand
Chawathe and Fellow (2002)	340 if $<$ 100 beds 450 if $>$ 100 beds	India
EPA (2002)	470-910 tipic 630	USA
Altin et al. (2003)	550-950 recommended 600	Turkey

4.2.3. Results

Table 4.11 shows the average percentage removal rate obtained by the tested systems: MBR with MF (0.45 μm), MBR with UF (0.01 μm) and SBR.

Table 4.11.: Removal rate for the main pollutants in Lagosanto tested pilots

Pollutant	**Removal rate, %**		
	MF	**UF**	**SBR**
SS	91.8	96.9	70.4
COD	91.5	91.1	72.7
Filtered COD		87.4	73.9
BOD_5	96.9	97.1	91.9
NH_4	97.8	28.2	25.6
P_{tot}	2.9	36	14
Total Surfactants		87.3	76.6
E. coli	99.8	99.993	60

Analysing the data is clear that MBR systems works better than the conventional biological system (SBR), the best results have always obtained with the UF membranes. The pores of these membranes, an average of 0.01 μm in fact can stop the suspended solids more effectively than the pores of a MF membrane and with the suspended solids a lot of pollutants.

It is important to put the attention on the permeate flux. In this flus, in fact, the organic matter derived only from the dissolved pollutants.

From a microbiological point of view, the MF membranes stopped an average of 2-2.5 log units of *E. coli*, while the UF membranes can always removed at least 4 log units ensuring an effluent with less than 10 *E. coli* 100 mL^{-1}.

The viruses were not analysed in this study. An analysis of those presents in WWs showed that they are usually 20-150 nm in size, so we can expect that the UF membranes tested, having a pore size lower than this value, are able to retain them.

Table 4.12.: Viruses present in HWWS and relative dimensions

Virus	**Dimensions, nm**	**Virus**	**Dimensions, nm**
Enterovirus	20-30	Norwalk	27-40
Adenovirus	70-80	Astrovirus	27-32
Rotavirus	60-80	Calicivirus	30-40
Parvovirus	20	Coronavirus	80-160
Reovirus	60-80		

The study on the somministration of carbamazepine and antibiotics shows that the presence in the HWWs is related to effective consumption: Obviously the consumption of these substances is variable over the year, as shown in figure 4.16 and

4.17.

For example, in samples taken in December, Carbamazepine and Cefazoline were always below their detection limit: unexpectedly, in winter months the average monthly consumption at the hospital are less than the monthly average on an annual basis.

Withdrawals in September and January, Carbamazepine and Cefazoline were higher in the permeate and clarified in relation to HWWs. This can be justified by the fact that in this period samples were instantaneous and not on the average of 24 hours. Moreover they not considered the effective hydraulic retention time of the pilot plant and this can cause some comparative errors.

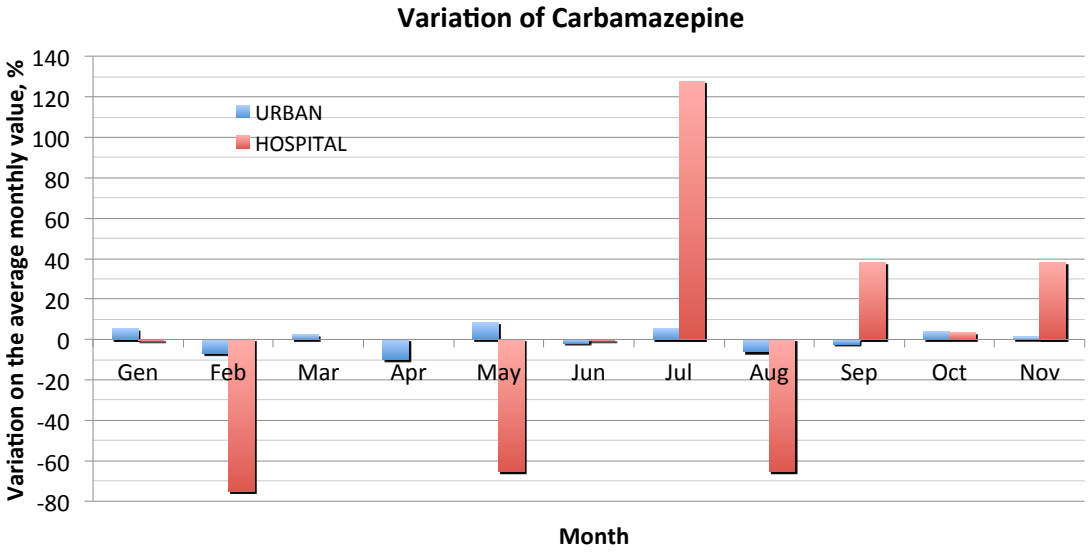


Figure 4.16.: Monthly variation on the Carbamazepine consumption in Urbans and Hospitals users in Lagosanto. Average values for Urbans users equal to 18.7 kg month^{-1} and for Hospitals users equal to 1.45 kg month^{-1}

4.3. CAS and MBR treatment in La Spezia

This section describes the experimental investigation carried out in La Spezia, northern Italy, studying the municipal WWTP. This plant is a CAS system that treats all the WWs derived from the town of La Spezia, including a the town hospital. In order to compare the different efficiency in removing PhCs a MBR pilot was studied in parallel with the CAS.

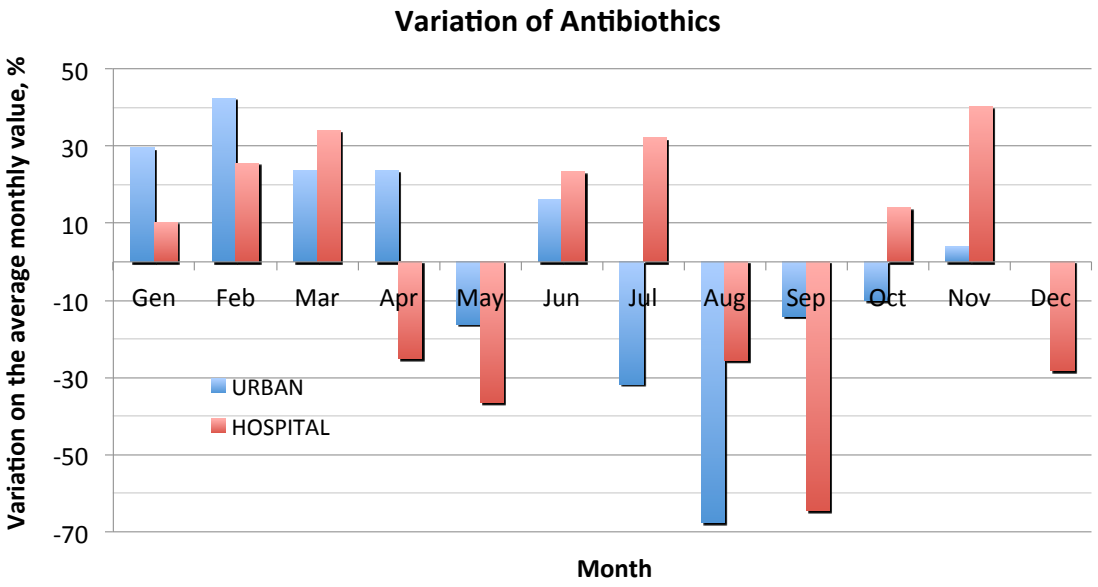


Figure 4.17.: Monthly variation on the antibiotics consumption in Urbans and Hospitals users in Lagosanto. Average values for Urban users equal to 0.31 kg month^{-1} and for Hospital users equal to 1.20 kg month^{-1}

La Spezia municipal WWTP (figure 4.18) is a CAS system built for 120 000 i.e. and consists in a conventional biological treatment that includes preliminary treatments (screening and gritting) and biological section. The final effluent is directly discharged into the sea without any kind of disinfection.

The average influent and effluent concentration for the main parameters in La Spezia WWTP are reported in table 4.13.

Table 4.13.: La Spezia WWTP average influent and effluent concentration for the main macro parameter

Parameter	**Influent**	**Effluent**
BOD_5, mg L^{-1}	356	3.3
COD, mg L^{-1}	576	23
$COD_{Soluble}$, mg L^{-1}	107	22
SS, mg L^{-1}	343	0.8
NH_4, mg L^{-1}	57	0.6

This experimental investigation was carried out in two month (May-June 2008) with a total of 12 samples analysed. In particular 4 samples for the influent WWs and 8 samples for the effluent of the two plant, two for CAS effluent, five for MBR effluent and finally one with the adding of ozone. For each sampling point a 24

Figure 4.18.: La Spezia WWTP

hours composite sample was taken.

The sampling point during this experimental investigation were the following:

- Influent CAS and MBR (the WWs for the influent were the same)
- Effluent CAS
- Effluent MBR
- Effluent MBR + O_3 (an experimental investigation were made also with a production of 8 g h^{-1} of O_3 with a contact time of 5 mins)

The analysed compounds in this experimental section were the 38 reported in table 4.14, moreover in table C.8 it is possible to compare all the different analytical results during the experimental investigation. Figure 4.16 presents all the percentage removal rate from the average values comparing CAS, MBR and MBR + O_3 treatments.

The main characteristics of the MBR pilot plant in La Spezia (figure 4.19) are reported in table 4.15.

Table 4.14.: Analysed compound in La Spezia

Amoxicillin	Ibuprofen
Atenolol	Idroclorotiazide
Atorvastatin	Ketoprofen
Bezafibrate	Lincomicin
Carbamazepine	Metotressate
Ciclofosfamide	Naproxen
Ciprofloxacin	Oleandomicin
Claritromicin	Ofloxacin
Clofibric acid	Omeprazole
Demetildiazepam	Ossitetraciclin
Diazepam	Ranitidine
Enalapril	Salbutamol
Deidro-Eritromicin + Eritromicin	Sildenafil
Diclofenac	Spiramicin
Estradiol	Sulfamethoxazole
Estrone	Tamoxifen
Etinilestradiol	Tilmicosin
Furosemide	Tilosine
Gemfibrozil	Vancomicin

(a) La Spezia MBR pilot plant (b) Puron membrane in La Spezia

Figure 4.19.: The MBR tested in La Spezia (Puron membrane)

The plant consists of three main tasks: denitrification tank, nitrification tank, and a final tank, dedicated to the membrane module filtration as reported in figure 4.20.

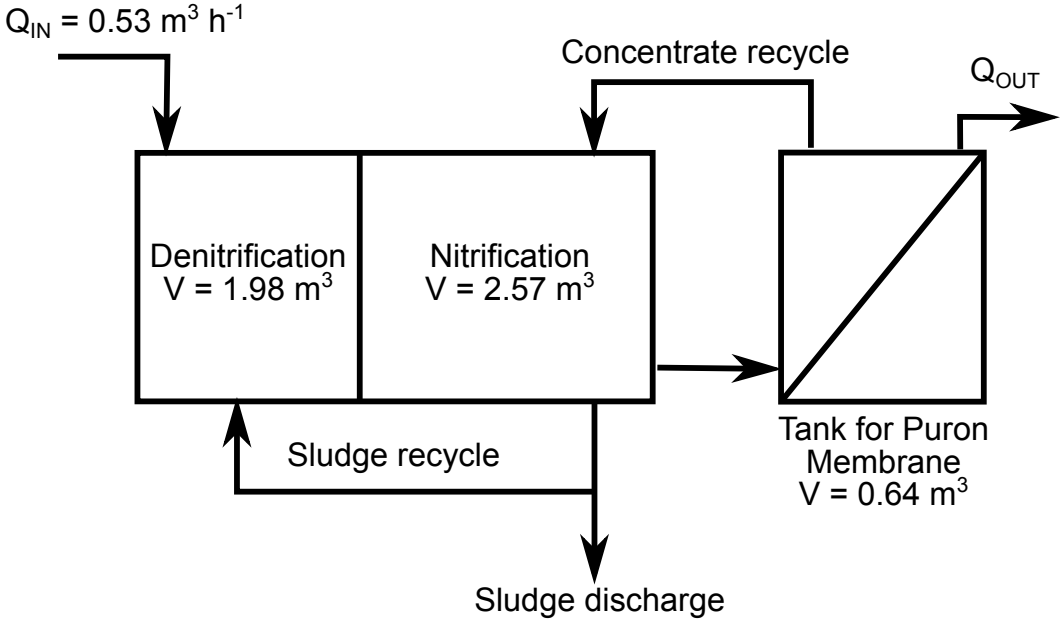


Figure 4.20.: MBR scheme in La Spezia

Table 4.15.: Characteristics of the MBR pilot plant studied in La Spezia

Parameter	**UF**
Period	May-June 2008
Membrane	Puron
Pore diameter, μm	0.05
Flow rate, m^3 h^{-1}	0.53
Superf. flux, L $m^{-2}h^{-1}$	22
Volume, m^3	Denitr. 1.98 - Nitr. 2.57
TMP pressure, bar	0.1
Tot. surf. membr., m^2	30
HRT, h	9
Sludge age, d	30
Membrane cleaning	1. Air insufflation
	2. Chemical cleaning

As clearly reported in tables C.8 and 4.16 the effective removal efficiency is not really constant for all the PhCs detected. CAS system may be sufficient to remove some micropollutants, but a MBR plant certainly improve the final efficiency. Moreover an additional treatment like O_3 transforms or degrades a lot of micropollutants and, for this way, reduces the final impact of the WWTP discharge.

Table 4.16.: La Spezia percentage removal rate from the average values. Comparison between CAS, MBR and MBR + O_3

Compound	MBR	CAS	MBR + O_3
Atenolol	91	80	97
Atorvastatin	98	81	100
Bezafibrate	82	88	99
Carbamazepine	2	4	0
Ciprofloxacin	88	20	39
Claritromicin	72	74	88
Demetildiazepam	42	21	20
Diazepam	43	0	8
Enalapril	100	100	100
Erytromicin	0	49	49
Diclofenac	53	12	26
Estrone	87	0	99
Furosemide	75	72	86
Gemfibrozil	97	69	97
Ibuprofen	100	98	100
Idroclorotiazide	61	0	0
Ketoprofene	92	73	97
Lincomicine	58	0	14
Naproxen	91	95	99
Oleandomicin	0	37	23
Ofloxacin	76	50	74
Ranitidin	88	97	94
Salbutamol	0	46	61
Sulfamethoxazole	79	93	68
Average	72	52	64

Summing all the detected concentration and doing a mass balance, it is possible to obtain the results in figure 4.21 where are shown the different load in g L^{-1} discharged before the relative treatment. In particular it is clear that a CAS system is able to remove the analysed compound but, one times more, a MBR seems to be able to improve the final efficiency. Another important aspect is related to the ozonation final step that, as all the AOP treatment is able to degrade or transform this micro contaminants and to improve the final efficiency.

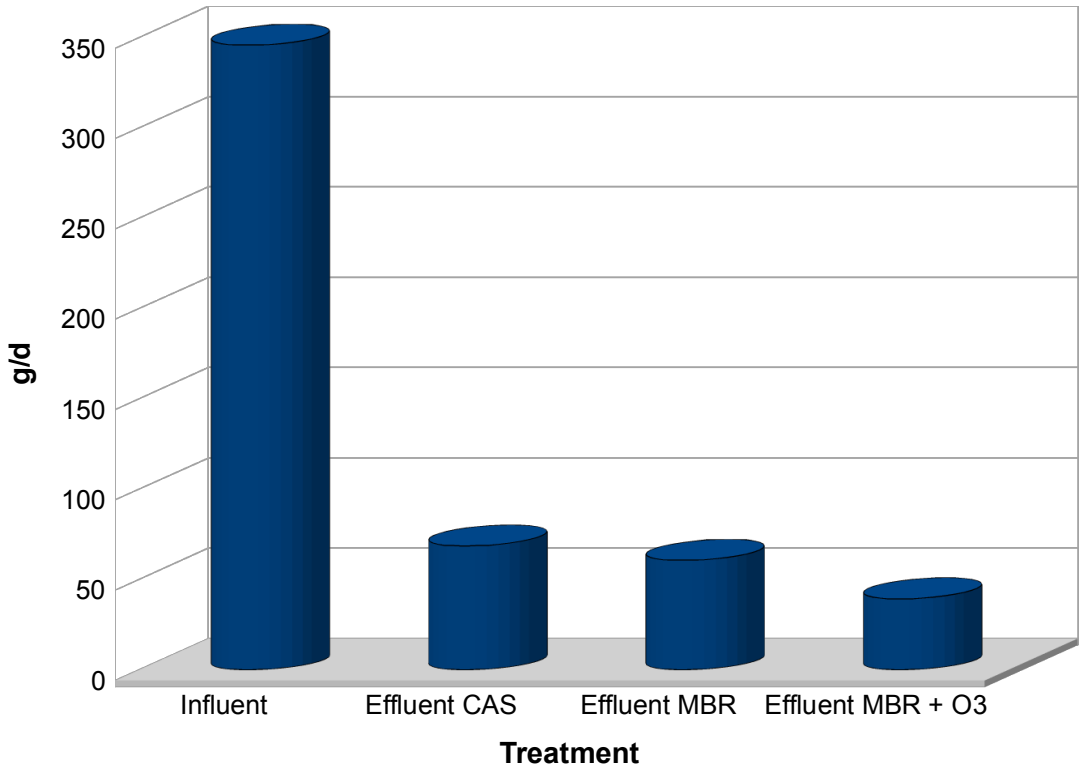


Figure 4.21.: Mass balance for the results obtained in the experimental investigation in La Spezia

Another important consideration is about the presence of the psychiatric drug Carbamazepine. This compound used primarily in the treatment of epilepsy and bipolar disorder, as well as trigeminal neuralgia is a recalcitrant compound present in high concentration in WWs and the more important fact is that, mainly for his stable chemical configuration (see figure 4.22) is stable on water and it resists to main WWs treatment and also at the ozone treatment.

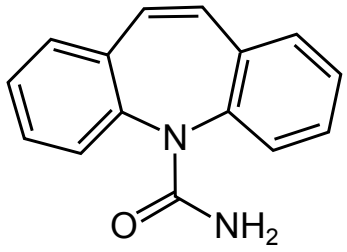


Figure 4.22.: Carbamazepine chemical structure

4.4. CAS treatment in Ferrara

This part of the study took place at the Ferrara municipal WWTP on march 2010. This WWTP consists of two separate but very similar lines: one for UWWs (on average 35 000 m^3d^{-1} in dry weather), the other for industrial ones (on average 15 000 m3 d^{-1} in dry weather). Urban line is shown in figure 4.24 and it includes preliminary treatments (screening and gritting), a biological treatment and a final disinfection performed by adding NaClO, at an average concentration of 10 mg L^{-1} with a contact time on average of 30 min. Then the final effluent is discharged into a surface water body belonging to the local channel network used in the hot season for agriculture irrigation.

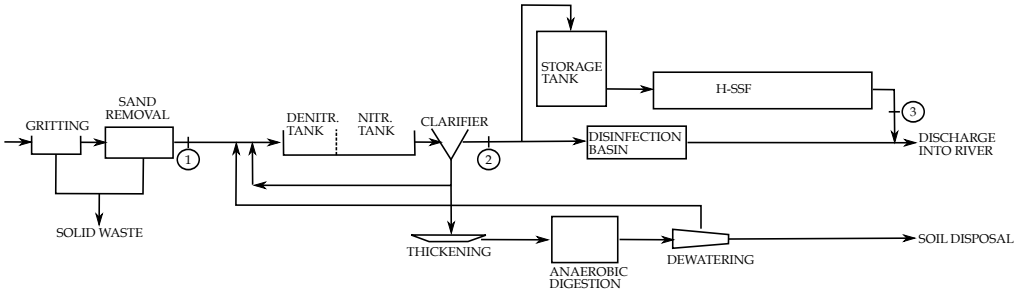
The biological treatment consists of a CAS system, including the steps of denitrification (V = 4000 m^3), nitrification (V = 6100 m^3) and then secondary sedimentation (V = 6000 m^3). It operates with an average hydraulic retention time (HRT) of 6 h, a sludge age of 8 d and a concentration of the mixed liquor of about 3.5 kg m^{-3}. An image of the Ferrara WWTP is reported in figure 4.23.

Table 4.17 reports the main parameter of WWs influent and effluent to the plant and figure 4.24 shows a scheme of the WWPT including the final polishing treatment consisting in a natural pilot plant CW.

Table 4.17.: WWs characterization macro-pollutants for influent and effluent from Ferrara WWTP

Parameter	**Influent**	**Effluent**
pH	7.6	7.2
COD, mg L^{-1}	109	45
BOD_5, mg L^{-1}	72	15
SS, mg L^{-1}	85	22
TKN, mg NH_4 L^{-1}	26	5
P_{tot}, mg L^{-1}	3	0.9

Figure 4.23.: Ferrara WWTP with the two lines for urban and industrial WWs



Legenda: 1: raw influent; 2: H-SSF bed influent (= WWTP secondary effluent); 3): H-SSF bed effluent.

Figure 4.24.: Flow scheme and sampling location (not in scale) of the Ferrara WWTP and the pilot station where the experimental campaign was carried out

4.4.1. PhCs removal rates in CAS

Literature data about the CAS systems and their capacity in removing PhCs are really diffuse and among them Ternes (1998), Stumpf et al. (1999), Golet et al. (2002); Rodriguez et al. (2003), Carballa et al. (2004), Kreuzinger et al. (2004), Paxeus (2004), Bendz et al. (2005), Carballa et al. (2005), Clara et al. (2005a), Clara et al. (2005b), Lindqvist et al. (2005), Tauxe-Wuersch et al. (2005), Vieno et al. (2005), Batt et al. (2006), Brown et al. (2006), Castiglioni et al. (2006), Lindberg

et al. (2006), Lishman et al. (2006), Nakada et al. (2006), Peng et al. (2006), Yu et al. (2006), Gobel et al. (2007), Gomez et al. (2007), Jones et al. (2007), Kimura et al. (2007), Ternes et al. (2007), Vieno et al. (2007a), Watkinson et al. (2007), Xu et al. (2007), Gulkowska et al. (2008), Ghosh et al. (2009), Kasprzyk-Hordern et al. (2009), Radjenovic et al. (2009), Santos et al. (2009), Zhou et al. (2009), Le-Minh et al. (2007), Sipma et al. (2010)) are the fruit of experimental investigations, generally carried out on full scale CAS systems treating real UWWs.

In general CAS system operated with a SRT of 10 d and at HRT of 7 h, with different plant configurations (aiming for carbon removal only, or including nitrification - denitrification steps as well as phosphate removal). For main details about the literature data and the mechanisms in removing PhCs from WWs see paragraph 5.1.2

The degree of environmental risk posed by the presence of these micropollutants is still under discussion. Safety threshold values have been defined for very few PhCs and only in single compound-single organism toxicity studies. Many compounds have not yet been extensively studied, and their toxicity data refer only to acute effects.

In particular, Cleuvers (2003) analysed the toxicity of diclofenac, carbamazepine and propranolol to Daphnia magna and found EC50 values equal to 68, 72 and 7.5 mg L^{-1}; these concentrations are significantly higher than the observed concentrations in the secondary effluent (ng L^{-1}).

Nevertheless, the environmental impact of a mixture of different PhCs could be more toxic than single compound alone. In fact, Daughton and Ternes (1999) and Flaherty and Dodson (2005) found that a mixture of PhCs exhibits unpredictable behaviour and can cause serious side effects such as deformities and increased mortality in Daphnia magna. This implies that, in the future, it would be prudent to begin monitoring of the most frequently administered and persistent compounds (the so-called target compounds).

4.4.2. Observed secondary effluent concentrations

Table 4.18 shows the observed concentrations of the PhCs of interest in the influent and effluent of the Ferrara WWTP. For each of the investigated pharmaceuticals, our

experimental data are invariably within the variability ranges found in the literature, thereby confirming that even though comparatively lower removal rates were found in the Ferrara CAS, the resulting secondary effluent had a similar quality to those reported in literature.

Moreover this table shows the corresponding percentage frequency of occurrence standard deviation. To see the complete analytical results see table C.9 at appendix C. The sampling data for all the results shown in table C.9 were march, 15, 16, 19 and 24, 2010 and all the samples were 4 hours composite samples.

Interestingly, in the secondary effluent, observed average concentrations for analgesics or anti-inflammatories and antibiotics ranged between 15 and 664 ng L^{-1} and between 10 and 1165 ng L^{-1} for all the other therapeutic classes. For many pharmaceuticals, the concentrations in secondary effluents are quite often greater than 50 ng L^{-1}.

Table 4.18.: Average values (ng L^{-1}, n=4) for the detected compounds in Ferrara WWTP raw influent, Ferrara WWTP effluent, corresponding percentage frequency of occurrence (f) and in brackets, standard deviation (SD)

Clas	**Compound**	**WWTP influent**		**WWTP effluent**	
		f, %	**Aver. (SD)**	**f, %**	**Aver. (SD)**
Analgesics	Acetaminophen	100	813 (270)	100	30 (20)
or	Codeine	100	107 (29)	100	66 (13)
anti-infl.	Diclofenac	100	439 (55)	100	284 (49)
	Ibuprofen	100	1026 (113)	100	81 (49)
	Indomethacine	100	160 (60)	100	98 (31)
	Ketoprofen	100	168 (27)	100	85 (21)
	Mefenamic acid	100	903 (252)	100	664 (209)
	Naproxen	100	832 (53)	100	178 (52)
	Phenylbutazone	100	106 (30)	100	52 (11)
	Propyphenazone	100	53 (18)	100	42 (20)
	Salicylic acid	100	498 (378)	100	118 (8)
Antibiotics	Azithromycin	100	112 (150)	100	131 (46)
	Chloramphenicol	100	19 (5)	–	–
	Ciprofloxacin	100	2212 (1085)	100	638 (349)

	Clarithromycin	100	308 (318)	100	284 (24)
	Enoxacin	100	102 (22)	100	61 (28)
	Erithromycin	75	58 (16)	50	23 (14)
	Metronidazole	100	42 (13)	100	28 (12)
	Nifuroxazide	100	52 (24)	50	18 (8)
	Norfloxacin	100	203 (72)	100	152 (13)
	Ofloxacin	100	1004 (822)	100	394 (138)
	Roxithromycin	75	84 (49)	100	29 (18)
	Spiramycin	75	81 (61)	100	31 (14)
	Sulfadiazine	100	22 (6)	100	17 (5)
	Sulfamethazine	100	18 (11)	75	12 (2)
	Sulfamethoxazole	100	443 (200)	100	214 (35)
	Tilmicosin	100	251 (183)	75	48 (29)
	Trimethoprim	100	58 (14)	100	40 (7)
Antidiabetic	Glibenclamide	100	87 (6)	100	55 (29)
Antihyp.	Enalapril	100	82 (12)	–	–
	Hydrochlorothiazide	100	2721 (1900)	100	1165 (199)
Barbiturates	Butalbital	100	133 (80)	100	101 (16)
	Pentobarbital	100	31 (11)	75	21 (6)
	Phenobarbital	100	207 (79)	100	138 (27)
Beta-	Clenbuterol	100	255 (29)	100	182 (37)
agonists	Salbutamol	100	13 (4)	75	14 (3)
Beta-	Atenolol	100	2081 (241)	100	734 (178)
blockers	Cerazolol	25	11	–	–
	Metoprolol	100	255 (29)	100	182 (37)
	Pindolol	25	11	–	–
	Propranolol	100	26 (14)	100	18 (6)
	Sotalol	100	534 (122)	100	323 (115)
	Timolol	100	14 (3)	25	12
Diuretic	Furosemide	100	423 (42)	100	274 (128)
Lipid	Atorvastatin	75	16 (4)	25	14
regulators	Bezafibrate	100	90 (27)	100	36 (17)

	Fenofibrate	25	18	25	13
	Gemfibrozil	100	200 (56)	100	108 (54)
	Mevastatin	100	173 (70)	100	83 (57)
	Pravastatin	100	114 (24)	100	54 (14)
Psychiatric	Carbamazepine	100	581 (389)	100	372 (69)
drugs	Diazepam	25	16	–	–
	Fluoxetine	100	106 (59)	75	57 (9)
	Lorazepam	100	219 (34)	100	120 (27)
	Paroxetine	100	41 (28)	100	13 (4)
Receptor	Cimetidine	100	47 (15)	100	31 (15)
antagonists	Famotidine	75	17 (6)	–	–
	Loratadine	75	16 (5)	–	–
	Ranitidine	100	111 (15)	100	78 (26)

Codeine is a compound scarcely referenced in previous studies, despite being the most widely used naturally occurring narcotic in worldwide medical treatment. It is an effective sedative, analgesic and antitussive agent. In this study, it was detected in raw WW at a mean concentration of 0.107 μg L^{-1} (greatly below the observed variability range of tables A.1...A.10 of 1.73-35 μg L^{-1}), and only 33% of this compound was removed after treatment (against 42-46% reported in literature).

Indomethacin was found at an average concentration of 0.160 μg L^{-1} in raw WW, in agreement with the observed variability range in raw UWWs reported in tables A.1...A.10.

Mefenamic acid is an hydrophobic compound which tends to sorb to sludge, and may undergo degradation. However, high variability in its removal rates has been observed by many Authors (Tauxe-Wuersch et al. (2005), Jones et al. (2007), Kimura et al. (2007)).

Concerning propyphenazone, its frequently low, and sometimes negative, removal rates can be ascribed to its hydrophilic nature ($\log K_{ow}$ =1.96) and chemical stability. Low removal rates for some beta-blockers (in this study: metoprolol, propranolol and sotalol), and even the occasionally measured negative removal (mainly atenolol and

metoprolol), have been found by other Authors (among them Bendz et al. (2005), Wick et al. (2009)).

Negative removals for macrolides including clarithromycin and erythromycin, are likely due to the release of these compounds from excreta during biological treatment, rather than presence of deconjugable metabolites: the load entering biological treatment is therefore underestimated when taking only the dissolved fraction and sorption to the suspended solids into account (Bryskier et al. (1993)).

Negative removal rates for carbamazepine are most likely due to enzymatic cleavage of the glucuronic conjugate of carbamazepine and the release of the parent compound in the treatment plant (Vieno et al. (2007a)).

Receptor antagonists including cimetidine, loratidine, famotidine and ranitidine have scarcely been studied and limited data (Gros et al. (2007), Radjenovic et al. (2009), Kasprzyk-Hordern et al. (2009)) are available for comparison with those found in this study. Furthermore, Radjenovic et al. (2009) found that their removal in CAS is unstable and varies over a wide range.

Although, clofibric acid is a common lipid regulator previously found to be quite persistent, it was not detected in this study. Similarly, Hijosa-Valsero et al. (2010b) failed to detect it in raw WWs.

Low elimination rates could be due to the fact that contaminants are present at very low concentrations in the influent, and their removal mechanisms barely have a chance to occur. For this reason, PhC concentrations in CAS secondary effluents merit comparison.

4.5. CW pilot plant in Ferrara - Standard usage

The CW pilot station in Ferrara has been operating since 2003 and it is directly fed by the effluent of the near WWTP. The investigated H-SSF CW is a long and narrow bed (28 x 1), filled with gravel (8-10 mm), with a depth ranging between 0.7 at the beginning and 1.75 m at the end of the bed and spontaneous plants and grass on turf (see figure 4.26).

In this experimental campaign, carried out on march and april 2010, the pilot plant feed was the effluent of the secondary clarifier, as shown in figure 4.24. It was

Figure 4.25.: Ferrara H-SSF pilot plant for the first investigation

pumped into a 10 m^3 tank placed at 3 m above the ground and fed by gravity to the pilot plants. The influent flow rate was set by a valve, regularly monotored by a flowmeter and kept at a constant flow rate of 8 m^3 d^{-1}. The HRT was about 1 d. The main parameters of the WWs before and after the CW treatment are shown in table 4.19, with the corresponding standard deviation (SD) in brackets. The reported values are the average ones on the basis of the data set referring to 2009 (n = 20-80, depending on the parameter).

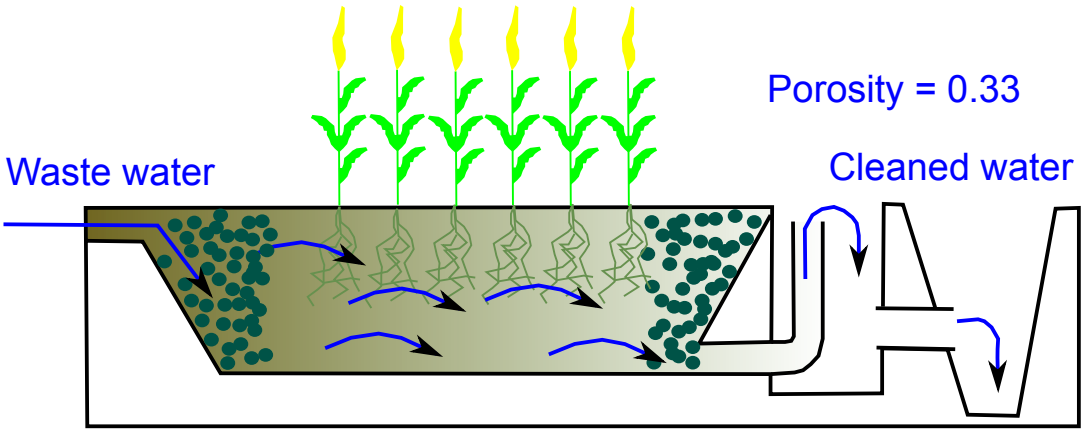


Figure 4.26.: Scheme of the tested natural system pilot plant

Table 4.19.: Characteristics of the investigated pilot plant and treatment performance during the first investigation

Parameter	**Pilot plant under study**
Length L, m	28
Width W, m	1
Aspect ratio, L:W	28:1
Average filling depth (max), m	1.2 (1.75)
Filling material, mm	Gravel, 8-10
Porosity, %	33
Plants	Spontaneous plants and grass on turf
Flow rate, m^3 d^{-1}	8
Design i.e.	53
Treatment performance (in/out)	
COD, mg L^{-1}	45(15)/11(6)
BOD_5, mg L^{-1}	18(10.8)/3 (1)
SS, mg L^{-1}	22(8)/4 (1)
TKN, mg NH_4 L^{-1}	5 (2)/3 (2)
Redox, mV	194 (40)/104 (25)
Sulphates, mg L^{-1}	60.5 (15)/63.5 (10)

4.5.1. PhCs removal rates in H-SSF

The present study investigates the ability and reliability of an H-SSF bed in removing the 73 PhCs of interest, from a secondary effluent feed to the pilot plant, as reported in figure 4.24. H-SSF systems seem to be effective at removing PhCs, despite the fact that the main removal mechanisms remain to be fully elucidated.

In general literature data refer to H-SSF beds of different sizes, aspect ratios (width:length), water depths, vegetation presence, hydraulic loading rate, hydraulic retention time, environmental conditions (mainly T and insolation) and soil matrix.

Most of them are laboratory or pilot plants, acting as secondary or tertiary treatments, fed by real WWs. Analyses were usually performed on 24 h composite water samples taken in dry periods. Not a lot of literature data are available on the removal of PhCs by natural treatments and among them ther are: Drewes et al. (2002), Matamoros and Bayona (2006), Ternes et al. (2007), Matamoros et al. (2009), Onesios et al. (2009), Hijosa-Valsero et al. (2010a), Hijosa-Valsero et al. (2010b).

For more details about the removing of PhCs with natural treatment see paragraph 5.1.8

4.5.2. Observed H-SSF effluent concentrations during the first investigation

Table 4.20 shows the average values an the relative standard deviation for the detected compounds in the H-SSF bed effluent. Moreover this table shows the corresponding percentage frequency of occurrence (f). To see the complete analytical results see table C.10 for the CW influent and table C.11 for the CW effluent. The sampling data for all the results shown in appendix C were: march, 30, april 1, 2 and 6, 2010 and all the samples were 4 hours composite samples. All the samples take into consideration the correct HRT of the natural systems.

Table 4.20.: Average values (ng L^{-1}, n=4) with standard deviation in H-SSF bed effluent, corresponding percentage frequency of occurrence (f)

Class	**Compound**	**H-SSF bed effluent**	
		f, %	**Aver. (SD)**
Analgesics	Acetaminophen	75	16 (6)
or	Codeine	100	28 (8)
anti-infl.	Diclofenac	100	271 (59)
	Ibuprofen	75	58 (14)
	Indomethacine	100	54 (17)
	Ketoprofen	100	69 (13)
	Mefenamic acid	100	533 (116)
	Naproxen	100	114 (64)
	Phenylbutazone	100	23 (8)
	Propyphenazone	75	50 (18)
	Salicylic acid	100	110 (5)
Antibiotics	Azithromycin	25	19
	Ciprofloxacin	100	208 (105)
	Clarithromycin	100	265 (57)
	Enoxacin	100	38 (26)
	Erithromycin	25	28
	Norfloxacin	100	74 (18)
	Ofloxacin	100	64 (17)

	Roxithromycin	100	42 (34)
	Spiramycin	50	12 (2)
	Sulfadiazine	100	20 (6)
	Sulfamethoxazole	100	180 (47)
	Tilmicosin	25	18
	Trimethoprim	100	25 (88)
Antidiabetic	Glibenclamide	100	42 (14)
Antihypertensive	Hydrochlorothiazide	100	432 (174)
Barbiturates	Butalbital	100	59 (25)
	Pentobarbital	50	12 (1)
	Phenobarbital	100	114 (33)
Beta-agonists	Clenbuterol	100	162 (24)
Beta-blockers	Atenolol	100	383 (151)
	Metoprolol	100	162 (24)
	Propranolol	25	11
	Sotalol	100	306 (114)
	Timolol	25	11
Diuretic	Furosemide	100	179 (85)
Lipid regulators	Bezafibrate	75	26 (3)
	Gemfibrozil	100	84 (46)
	Mevastatin	100	39 (16)
	Pravastatin	100	26 (12)
Psychiatric drugs	Carbamazepine	100	387 (55)
	Fluoxetine	100	44 (32)
	Lorazepam	100	105 825)
Receptor antagonists	Cimetidine	100	23 (11)
	Ranitidine	100	46 (22)

4.6. CW pilot plant in Ferrara - Increasing of the PhCs influent concentration

In order to confirm the buffering step of a final natural polishing treatment this experimental investigation was carried out with the aim to observe the behaviour of some common antibiotics: Ciprofloxacin, Sulphametoxazole and Trimethoprin during the passage through a H-SSF pilot plant.

Every 5 days, 1 m^3 of tap water was spiked with 2.5 g of Ciprofloxacin, 2 g of Sulphametoxazole and 0.4 g of Trimethoprin. This mixture was homogenized and then added to the secondary effluent, using a peristaltic pump, and fed to the pilot plant.

The characteristics of the studied pilot plant (figure 4.27) are reported in table 4.21.

Figure 4.27.: Ferrara H-SSF pilot plant for the second investigation

The pilot plant consists of a vegetated (*Phragmites australis*) H-SSF bed (12 m x 2.5 m x 0.8 m), filled by gravel (8-10 mm), located at the municipal WWTP of Ferrara. It is fed by the secondary biological effluent, at a constant flow rate of 8 m^3 d^{-1}.

Twelve composite water samples have been withdrawn at the inlet and the outlet of the bed and performed for the three antibiotics, during the observation period March-June 2010.

All the twelve samples were taken in dry season in order to avoid a possible dilution with the rain water. The samples were 4 hours composite and each one takes in consideration the correct HRT of the system. They were taken in glass cleaned

bottle and analysed at the Department of Analytical Chemistry of the University of Ferrara.

Table 4.21.: Characteristics of the investigated pilot plant during the second investigation

Parameter	**Pilot plant under study**
Length L, m	12
Width W, m	2.5
Aspect ratio, L:W	12:2.5
Average filling depth, m	0.8
Filling material, mm	Gravel, 8-10
Porosity, %	33
Plants	*Phragmites australis*
Flow rate, m^3 d^{-1}	8
Design i.e.	56

4.6.1. Observed H-SSF effluent concentrations during the second investigation

Figures 4.28, 4.29 and 4.30 show concentration of the three PhCs in the influent and in the effluent of the H-SSF bed.

The variability range of the influent concentration has been really wide for Sulphamethoxazole (14-350 μg L^{-1}), modest for Trimethoprim (4-16 μg L^{-1})and quite small for Ciprofloxacin (0.26-4μg L^{-1}). For each investigated compound, the variability range of the effluent concentration, has been always smaller than the corresponding range in the influent.

The three antibiotics have had a different behavior, passing through the H-SSF bed: Sulphamethoxazole was scarcely removed (20% on average), while Trimethoprim and Ciprofloxacin had high average removal rates: respectively of 56%(SD=17) and 84% (SD=7).

Watching the figure and the complete results reported in appendix C, in table C.12, it is clear that also at hight concentration of these compounds CW can have an important buffering function, and it is able to reduce the concentration of the influent pollutant. Only for the Sulphamethoxazole the effluent concentration is highest than the influent because an uncorrect calculation of the HRT or an effective release of this antibiotic.

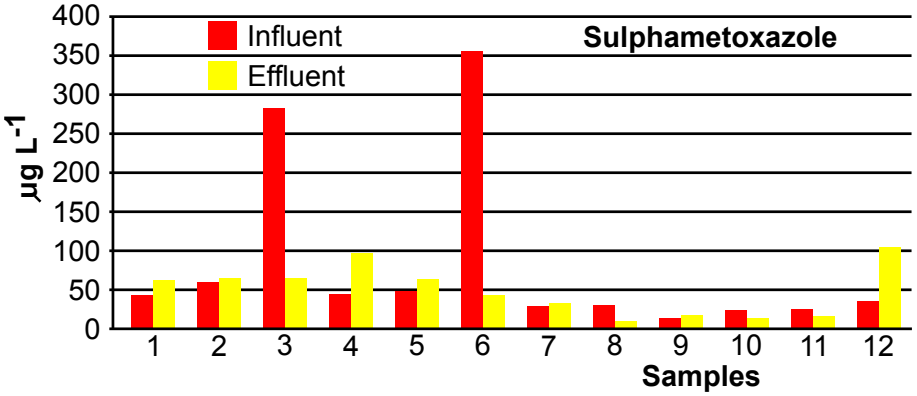


Figure 4.28.: Sulphamethoxazole removing in CW during the second investigation

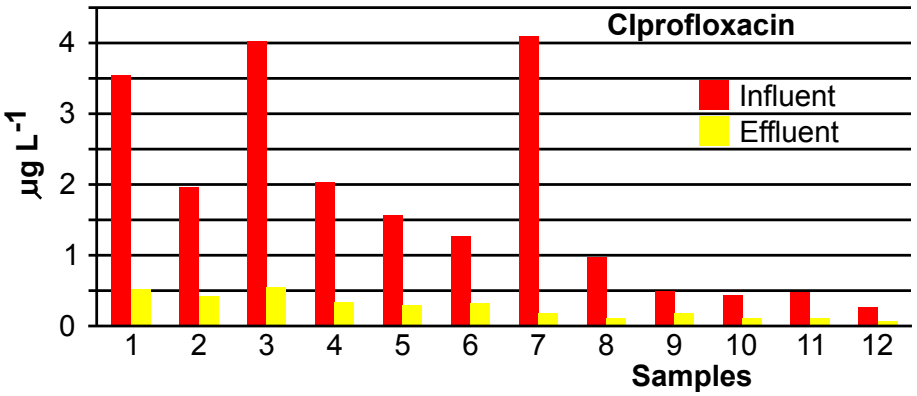


Figure 4.29.: Ciprofloxacin removing in CW during the second investigation

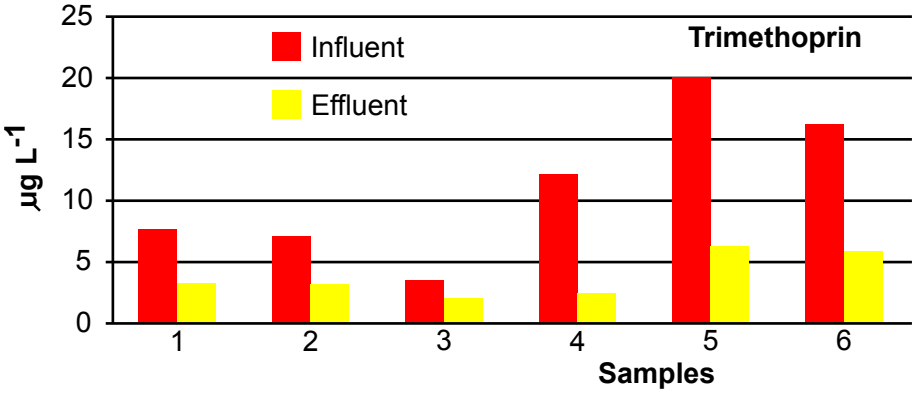


Figure 4.30.: Trimethoprim removing in CW during the second investigation

4.7. Discussion

This chapter presents all the experimental investigations carried out during this Ph.D. research and a summary of all the works is reported in appendix B.

The treated technologies here reported are different and the starting point were a simple disinfection of the raw HWWs with PAA or NaClO for those situation where is not present a WWTP able to treat this specific WWs. The successive experimentation regarded the comparison between CAS, MBR and CW system, with a small experimentation with ozone before MBR treatment in order to see the effective improvement of the water quality with this strong oxidant.

In general, the final results of each experimental investigation, shown that a multi-barrier system can improve the water quality guaranteeing an hight removal efficiency mainly in those pollutant (like micropollutant and PhCs) that are present in very small quantity in WWs. This because the typical WWTP are able to remove the carbonaceous fraction (like COD, BOD_5) and the nutrients (N and P) present in WWs but not all the pollutants that present concentration with magnitudo order of μg L^{-1} or ng L^{-1}. This because the typical biological treatment needs time and quantity to develop bacterial and biomasses able to degrade and transforms also the micro-compounds.

Section 4.2 reported only the results from an experimental investigation about MBR in HWWs from a *typical* point of view, in substance mainly studying the macroparameter and the problem connected with the hospital effluent.

The successive section (from section 4.3 to section 4.6) instead shown the study about PhCs in different pilot plants CAS, MBR and CW in order to focus the attention in these important technologies.

The last investigation carried out (section 4.6) had the aim to assess CW ability in removing three antibiotics (Sulphametoxazole, Trimethoprin and Ciprofloxacin), commonly used. It was found that there average removal rates decrease in the order Ciprofloxacin > Trimethoprin > Sulphametoxazole.

4.7.1. Removal rate by CAS and H-SSF

This section describes and discusses the connection between CAS and natural technologies and in particular the use of the natural step at the end of the biological treatment, in order to guarantee a buffering, able to stop pollutant and reduce the final discharge impact in waters bodies.

Figure 4.31 reports the percentage removal rates for the 11 investigated therapeutic classes, to the CAS system and to the polishing stage. In this figure the two parts of each rectangle represent the contribution of the CAS system and the H-SSF bed in the removing of all the compounds of a class.

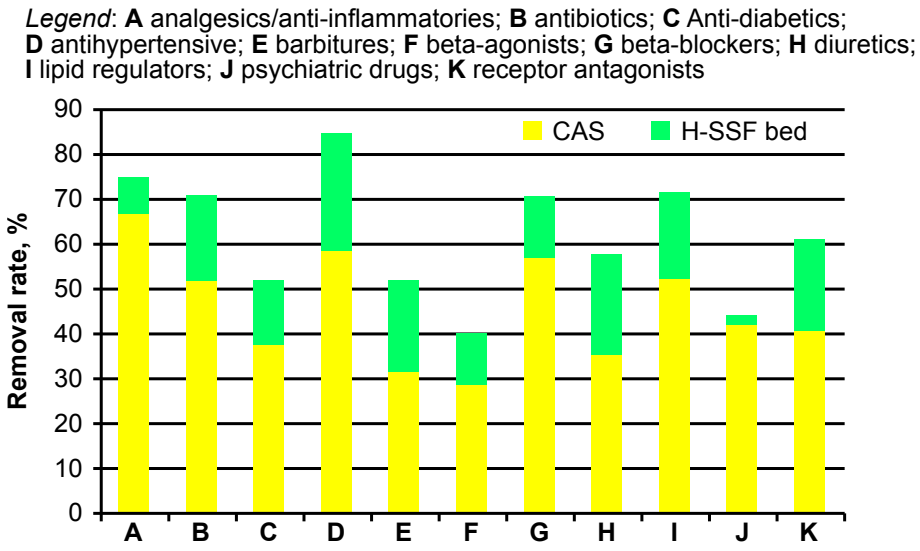


Figure 4.31.: Overall average removal rates for the 11 investigated therapeutic classes

This figure reports the overall average removal rates η_h for the therapeutic classes of interest as well as the contributes of the two steps j in the removal performances. These removal rates have been obtained applying eq. 4.5.

$$\eta_h|_j = \frac{\sum_{i(h)} c_{i_{average,inf}} - \sum_{i(h)} c_{i_{average,eff}}}{\sum_{i(h)} c_{i_{average,raw}}}|_j \times 100 \tag{4.5}$$

where i(h) represents each of the PhCs belonging to the therapeutic classes h, $c_{average}$ is the average concentration of the generic compound i in the influent (pedix inf) or in the effluent (pedix eff) of the treatment step j or in the raw influent to CAS system (pedix raw).

The H-SSF bed manages to fatherly reduce the overall concentration of each class, improving the quality of the final polished effluent. Its contribute varies between 1 to 26 %, on average 16 % with a standard deviation equal to 7.

An analysis and a comparison of the mass loadings for each of the therapeutic classes of interest in raw UWWs, in the secondary effluent and in the polished one may better show this capacity. Table 4.22 reports the mass loadings, referring to a small communities of 1000 inhabitants, on the basis of the observed average concentration discussed above. The main contributes are due to analgesics and anti - inflammatories, followed by antibiotics. In raw UWWs the mass loading amounts to 5.39 g 1000^{-1} i.e.$^{-1}$ d^{-1}, after a CAS including nitrification - denitrification steps the mass loadings lowers to 2.38 g 1000^{-1} i.e.$^{-1}$ d^{-1} and after a further subsurface flow system treatment reduces to 1.55 g 1000^{-1} i.e.$^{-1}$ d^{-1}.

Table 4.22.: Specific mass loadings of an urban settlement of 1000 i.e., in case of a discharge of raw UWWs, secondary effluent and polished one by means of H-SSF bed. Data reported in g 1000^{-1} i.e.$^{-1}$ d^{-1}

Class	**Raw UWWs**	**Secondary effl.**	**Polishing effl.**
Analgesics/anti-infl.	1.47	0.49	0.37
Antibiotics	1.44	0.70	0.42
Antidiabetics	0.03	0.02	0.01
Antihypertensives	0.81	0.34	0.12
Barbitures	0.11	0.07	0.05
Beta-agonists	0.08	0.06	0.05
Beta-blockers	0.84	0.36	0.25
Diuretics	0.12	0.08	0.05
Lipid regulators	0.17	0.08	0.05
Psychiatric drugs	0.27	0.16	0.15
Beta-antagonists	0.05	0.03	0.02
Total PhCs	**5.39**	**2.38**	**1.55**

The reported results show that a final natural polishing treatment is able to favour different removal pathways which become necessary due to the great variability of the contaminants of interest.

If the receiving river is an effluent dominant water surface body, becomes necessary to improve the quality of the discharge in order to reduce the long term environmental impact.

CW require high surface i.e.$^{-1}$ ratio, these *natural* polishing treatments represent

adequate solution for small communities or the last treatment step for the dedicated treatment of specific users, such as heath care structures or HWWs where the concentrations of such micropollutants should be more carefully removed. Matamoros et al. (2008) found that when these natural tertiary treatments are compared with advanced oxidation treatments like ozonation (Zwiener and Frimmel (2000) or MBR (Kimura et al. (2005)) the PhCs removal efficiencies are similar.

CHAPTER 5

Technologies and management

This Chapter describes the different technologies used to remove the PhCs from WWs. All these considerations derived from literature research and from the experience done during this Ph.D., in fact this research work, made from the management of numerous pilot plant, working with different scenarios.

A really interesting explanation of the historical evolution of the different step of WWTP, is reported in Ternes et al. (2004b) where the figure 5.1 is an important starting point:

In the 1950s, WWTPs were designed only for biological oxygen demand (BOD) removal. In the 1960s, chemical phosphate precipitation was introduced to reduce the phosphorus load being discharged. In the 1970s, processes were implemented to convert ammonia (primarily derived from urine, and toxic to fish) to nitrate (a less toxic form of nitrogen). In the 1980s, engineers put in place methods to partially convert nitrate to molecular nitrogen. Enhanced biological phosphate elimination was introduced in the 1990s when an anaerobic zone was implemented.

5.1. Overview of the removal processes

The removal of PhCs during WWs treatment can occur by means of the following mechanisms:

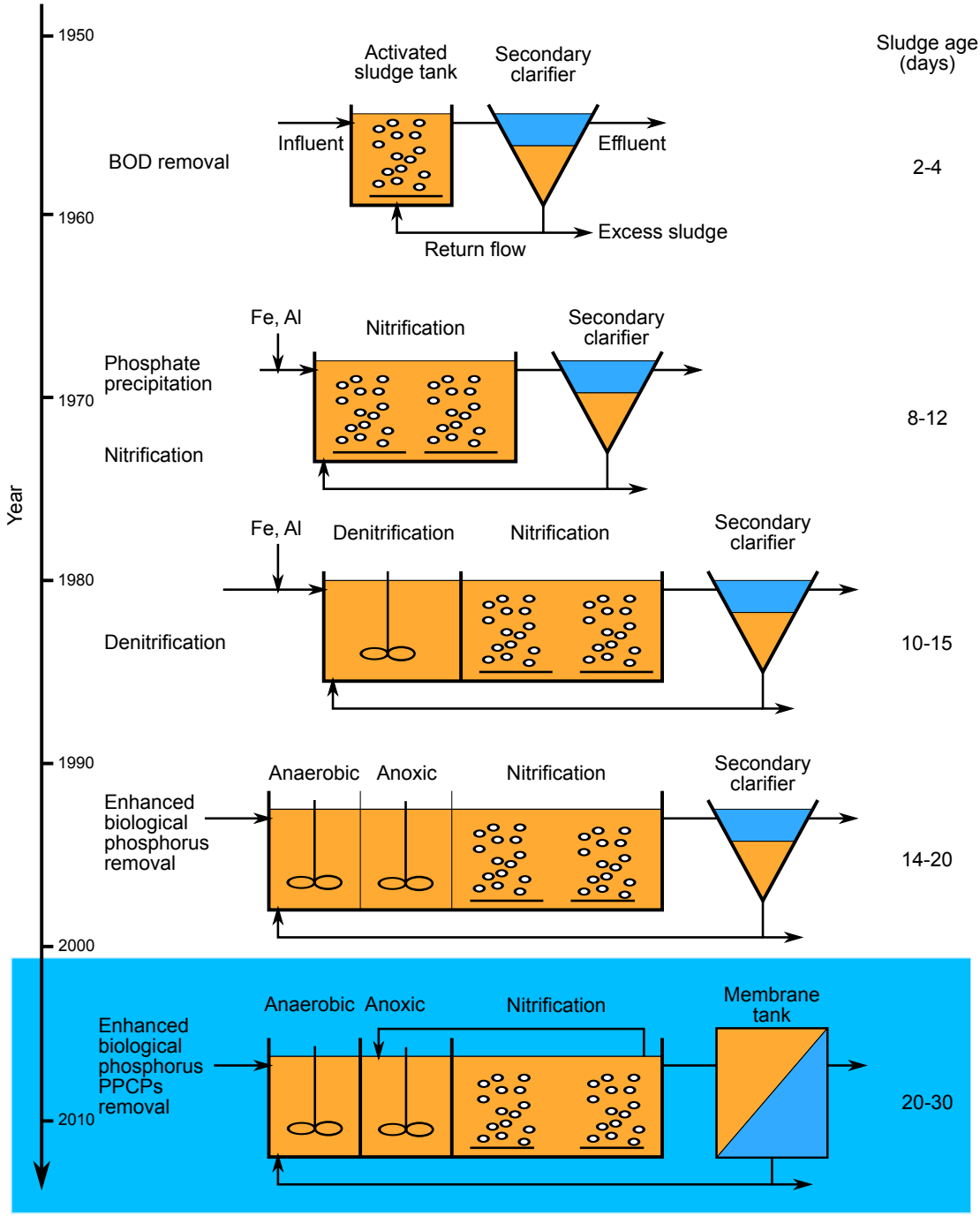


Figure 5.1.: Historical development of activated sludge treatment in Europe. Imagine adapted from Ternes et al. (2004b)

- **Biological degradation**: sludge age has shown to be a major factor influencing the palette of chemical structures being microbiologically transformed. The observed degradation rates of various compounds differ significantly without showing any evident correlation to specific molecular structure: currently no quantitative structure activity relationship (QSAR) can be identified. The observed removal rates vary form very fast (e.g. estradiol, paracetamol) to zero (e.g. carbamazepine, diatrizoate). Therefore the degradation of each compound has to be determined experimentally (i.e. the rate constant related to sludge concentration and sludge age).

- **Sorption onto sludge** issues in a removal of the sorbed share out of the water phase and into the sludge processing path. Sorption behaviour can be estimated with the help of the sorption coefficient (K_d), a value depending mainly from characteristics of the compound, as well as of the sludge. Currently no correlation of the observed K_d with literature value (e.g. octanol water partitioning K_{OW} or partitioning to soil organic carbon K_{OC}) could be found: besides hydrophobic also electrostatic interactions are relevant for sorption onto activated sludge. Nevertheless for the musk fragrances the high K_{OW} correlated with a high K_d. Therefore, the sorption coefficient has to be measured for each compound and for each sludge type (e.g. primary, secondary, digested). Concerning the elimination from the water phase of UWWs, sorption can be neglected for compounds with a $K_d < 500$ L $kgSS^{-1}$.

- **Stripping** is not a relevant process for PhCs, since these exhibit a fairly good solubility and therefore a low gas-water-partitioning coefficient. WWTPs equipped with mechanical surface or coarse bubble aeration (e.g. MBR) represent an exception, due to the higher amount of air getting in contact with the WWs compared to fine bubble aeration: in this case volatile compounds (e.g. musk fragrances) can be stripped in significant amounts.

- **Chemical oxidation**: ozonation of the effluent, has confirmed, being a feasible polishing step for biologically treated wastewater with the potential of eliminating a wide variety of PPCPs.

In conclusion of this rapid focus on removal mechanisms, it is possible to see, that biological degradation and sorption are the main mechanisms for PPCPs removal during municipal WWs treatment. Ozonation is an interesting option for advanced treatment.

On the basis of the literature data, the capacity in removing pharmaceuticals compounds from WWs, depends on the chemical and physical properties of the specific compound.

While it can be said that the effect of primary treatment of sedimentation is very poor, the effectiveness of biological treatments varies with the type of contaminant.

As reported, there is no specific treatment able to remove, at high percentage, all kinds of micropollutants typically found in HWWs, due to their differing behaviour during treatments. In addition, removal efficiencies may vary from hot seasons to cold ones as reported in Jones et al. (2005b), Castiglioni et al. (2006), Lindberg et al. (2006), Lishman et al. (2006), Pauwels and Verstraete (2006), Matamoros et al. (2008) and Miege et al. (2008).

HWWs are generally co-treated with UWWs in conventional WWTPs and are then released into the environment. However, many PhCs are resistant to conventional treatments. Elimination efficiencies of these compounds in municipal WWTPs have been investigated recently by many authors like among them Carballa et al. (2004), Nakada et al. (2006), Batt et al. (2007), Oppenheimer et al. (2007), Santos et al. (2007), Vieno et al. (2007a), Terzic et al. (2008), Teske and Arnold (2008). Considering all the PhCs investigated, the overall average removal rates range between 10 and 90%. Different operational configurations should be developed and calibrated, thus generating the potential for practitioners to be informed about the financial aspects and overall risks associated with putative treatments of HWWs (Pauwels and Verstraete (2006)).

Source controls could be an effective precautionary measure and an alternative to end-of-pipe upgrading of treatment plants. As reported below, administrated PhCs are excreted from the human body via faeces and urine at a percentage which changes with the compounds. Separate collection of urine, can contribute to keeping these substances away from WWs, but it will not be the perfect solution. Urine source separation (Nomix technology) can be more conveniently adopted for other

reasons, for instance water pollution control with respect to nutrients. In this case, facilitated removal of pharmaceuticals could have very welcome side effects (Lienert et al. (2007a)). A correct management of hospital effluents, requires that discharges from toilets used by patients undergoing nuclear medicine therapy must be collected into separated tanks and treated in the required way, thus avoiding immission of radioactive compounds into the hospital sewage and from there into the public sewage (Emilia-Romagna (2009)).

A dedicate treatment for HWWs is always a good solution, especially in the case of a large hospital in a rural area, where its treated effluent will be indirectly reused for irrigation after its discharge into a surface water body.

A co-treatment with UWWs at a municipal WWTP is a common practice, but it has several drawbacks. In the first place, dilution of HWWs with UWWs is not a correct practice, as some substances in the hospital effluents may result in inhibition of the biomass and reduce the removal efficiency. Different WWs treatments may be appropriate only for some groups of compounds, depending on their chemical-physical characteristics. Next section gives an overview of the removal capacity of different treatment steps.

Larsen et al. (2004) explain that parameters influencing the degradation efficiency are not yet fully understood; in the focus of current research are sludge age (solids retention time, figure 5.2), substrate availability (substrate inhibition), redox conditions (aerobic, anoxic or anaerobic), sorption (as competitive reaction), and reactor configuration (number of cascaded compartments, biofilm growth surface, sand filtration).

5.1.1. Physico-chemical treatments

Ternes and Joss (2006) explane that a coagulation - flocculation process was generally found to be unable to remove PPCPs.

On the contrary, adsorption by activated carbons (both powdered and granular forms: respectively PAC and GAC) has a great potential for the removal of trace emerging contaminants, in particular non-polar compounds with a $\log K_{ow} > 2$. PAC dose or GAC regeneration or replacement are critical for excellent removal rates (Snyder et al. (2006), Bolong et al. (2009)).

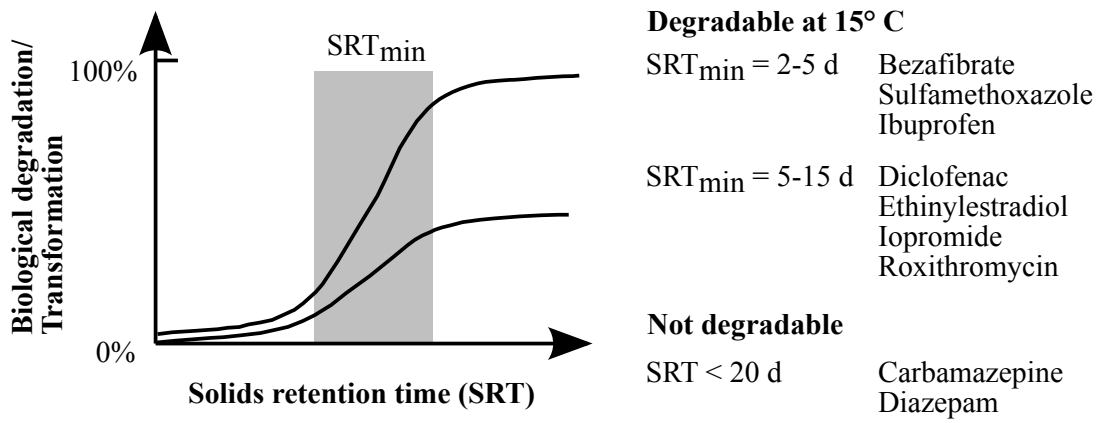


Figure 5.2.: Biological degradation resp. transformation of a micropollutant depends on the aerobic solids retention time, SRT (adapted from Larsen et al. (2004))

Schafer et al. (2003) found that the potential of endocrine disrupter compounds removal by powdered activated carbon, may be up to 90% (at 5 mg L^{-1} of PAC and 4 hour contact time); Snyder et al. (2006) examined 66 PPCPs and only 9 of them had a removal efficiency less than 50% at a dose of 5 mg L^{-1} PAC with 5 h of contact time. It is important to consider the unavoidable carbon regeneration/disposal issue. PAC must be disposed of through land, filling, or other solids handling, while spent GAC must either be disposed of or regenerated. Thermal regeneration of GAC requires a significant quantity of energy, which may lead indirectly to greater environmental risks than the presence of trace micropollutants. A cost benefit analysis should take these factors into account.

Suarez et al. (2009) explain that coagulation-flocculation can be a suitable pre-treatment option for HWWs in order to partially assimilate their physico- chemical characteristics to that of UWWs. Concentrations of suspended solids, which showed to be up to three fold higher in the hospital effluent considered compared to municipal sewage, could be very efficiently removed during coagulation- flocculation. Similarly, hospital effluents were in some occasion significantly stronger polluted with total COD compared to municipal sewage, which was also partially removed during pre-treatment.

The lipophilic character of a substance play an important role in the removal rate with this technologies and those substances that presents strong lipophilic character shows highest efficiencies.

5.1.2. Biological treatments

There are five major groups of processes used for WWs treatments (Metcalfe and Eddy (1991)) and they are: aerobic processes, anoxic processes, anaerobic processes, combined aerobic, anoxic, and anaerobic processes, and pond processes.

The individual processes are further subdivided, depending on whether treatment is accomplished in suspended-growth systems, attached-growth systems, or combinations thereof.

It should be noted that all of the biological processes used for the treatment of WWs, are derived from processes occurring in nature.

As reported in Metcalfe and Eddy (1991), the principal applications of these processes are for:

1. the removal of the carbonaceous organic matter in WWs, usually measured as BOD_5, total organic carbon (TOC), or chemical oxygen demand (COD);
2. nitrification;
3. denitrification;
4. phosphorus removal;
5. waste stabilization

Several studies have examined the effectiveness of conventional activated sludge processes (CAS) and UF MBR in removing emerging contaminants (among them Clara et al. (2005a), Kimura et al. (2007) and Radjenovic et al. (2009)). The main aspects they investigated have been: role of SRT in removal efficiency and role of nitrifying bacteria in biodegradation. It was found that:

- Removal efficiencies were enhanced for several investigated contaminants at longer SRT ($>$ 15 d), with threshold SRT for some compounds, beyond which removal rates did not improve. Longer SRT allows for the establishment of slower growing bacteria (i.e. nitrifying bacteria) which in turn provide a more diverse community of microorganisms with broader physiological capabilities, enhance metabolic and co-metabolic processes which also affect recalcitrant compounds and promote a more complete mineralization (Kreuzinger et al.

(2004), Clara et al. (2005a); Clara et al. (2005b); Daigger et al. (2005); Oppenheimer et al. (2007)).

- For some compounds (ibuprofen, methyl paraben, galaxolide, triclosan, caffeine) there is no significant difference in removal efficiencies by CAS and MBR (Oppenheimer et al. (2007)), while for many other pollutants experimental investigations have demonstrated that MBR technology generally outperforms the CAS treatment in their removal from WWs, the removal efficiency by MBR was 30-50% greater than in CAS. Moreover the elimination of some compounds that showed recalcitrant for the CAS treatment, such as mefenamic acid, indomethacin, diclofenac, and gemfibrozil, was significantly improved in the MBRs at up to around 40, 40, 65, 32-42% (Ternes and Joss (2006); Bouju et al. (2008); Reif et al. (2008); Radjenovic et al. (2009)). Some persistent substances as carbamazepine were not removed by either MBR or CAS treatment.

- No relationship was found between the structures of the investigated compounds and their removal during WWs treatment. The range of variation of the efficiency of removal by MBR was small for most of the compounds, while in conventional treatments, greater fluctuations were observed, and removal efficiency was found to be much more sensitive under operating conditions (pH, redox potential, temperature, flow rate, etc) (Ternes and Joss (2006); Radjenovic et al. (2007)).

- The constant of biological degradation k_{biol} provides information about the tendency of the compounds to be removed by biological processes. If $k_{biol} < 0.1$ L gSS^{-1} d^{-1} degradation is in general $< 20\%$, if $k_{biol} > 10$ L gSS^{-1} d^{-1} the biodegradation is greater than 90% (Ternes and Joss, 2006). The table in the appendix reports the values, or the range of values, for many pharmaceuticals and other emerging contaminants, found for MBR and CAS systems.

- Dividing the available reactor volume into reactor cascades can significantly improve performance (Joss et al. (2006), Ternes and Joss (2006)).

- Batt et al. (2006) and Marttinen et al. (2003) found that nitrifying bacteria

have a key role in the biodegradation of pharmaceuticals in WWTP that are operated at higher SRTs. Miege et al. (2008) found that in biological systems with nitrogen treatment the removal efficiency of PPCPs is in general higher than for other treatments such as submerged biofilters or fixed biomass reactors.

- All the investigations agree in considering secondary biological treatments to be an effective barrier for most emerging compounds.

Resuming the main PhC removal mechanisms in CAS processes are a combination of biodegradation due to suspended biomass and sorption onto particles, flocks and then sludge. Many factors, other than the characteristics of the compounds themselves, affect the elimination rate of PhCs. The most important are design and operational factors such as SRT, HRT, water temperature, pH, load factor to the biological reactor, configuration and type of plant. In general, biological degradation is favoured by higher SRTs, although not all PhCs exhibited a critical SRT. Indeed, although Clara et al. (2005a) found that a SRT $>$ 10 d is needed for some biodegradable PhCs to achieve low effluent concentrations, other studies (Joss et al. (2005), Vieno et al. (2007a)) noticed no clear correlation between elimination rate and SRT.

A minimum HRT is also important, as it allows the degradation of PhCs. Rain events in areas with combined sewer systems compromised the removal efficiencies of CAS, presumably due to shorter HRTs and washout of certain microorganisms (Vieno et al. (2007a)). Biological reactions are greatly affected by temperature, and lower efficiencies have been observed during winter seasons in colder climates (Vieno et al. (2005)). However, it is still unclear whether temperature dependencies commonly observed for biological treatment also apply to the transformation of antibiotics or micropollutants in general (Ternes (1998), Tauxe-Wuersch et al. (2005), Gobel et al. (2007)). High removal rates of PhCs have been suggested to occur in WWTPs with high levels of nitrogen removal (Clara et al. (2005a), Batt et al. (2006)), although Vieno et al. (2007a) found that nitrifying reactors do not enhance the elimination of fluoroquinolone antibiotics, beta - blockers or carbamazepine.

Sorption to activated sludge was also found to be of minor importance for those compounds, with an estimated sorption constant K_d of between 114 and 460 L kg^{-1}.

In general, less than 10% of for compounds with $K_d < 500$ L kg^{-1} elimination by sorption onto activated sludge at an average sludge production of 200 g m^3 is less than 10% (Ternes et al. (2004a)).

Analysis of the influence of the redox conditions on PhC removal in the conventional treatments, has not yet been extensively considered. In a CAS system, this parameter varies greatly between the different compartments of nitrification (> 100mV) and denitrification (from about -200 to +100 mV).

This behaviour of PhCs in CAS system can be correlated to:

- the configuration of the biological reactor: beta-blockers, for example, seem to be eliminated to a lower degree in denitrification processes, as compared to activated sludge treatment, designed for the removal of biologically degradable organic matter, or to ditch oxidation processes (Vieno et al. (2007a));

- the presence of deconjugates which interfere to a viable extent with biological transformation of the deconjugated compounds.

An interesting representation of the fate of the organic contaminant during sewage effluent treatment is done from Rogers (1996). This article explains that organic contaminants in effluent streams can be removed by a wide range of different processes, as reported in figure 5.3. However, most of these techniques are only appropriate to specific effluents of industrial origin and are expensive. In order to predict whether or not a particular organic contaminant is likely to be accumulated by the sewage sludge matrix, the following factors need to be taken into account.

- sorption (onto solid surface or association with fats and oils)

- chemical degradation (abiotic processes e.g. hydrolysis)

- biodegradation

- volatilisation

Sorption and volatilisation are physical processes and their importance for specific contaminants can be predicted using physicochemical data. During primary sedimentation, hydrophobic contaminants may partition onto settled primary sludge

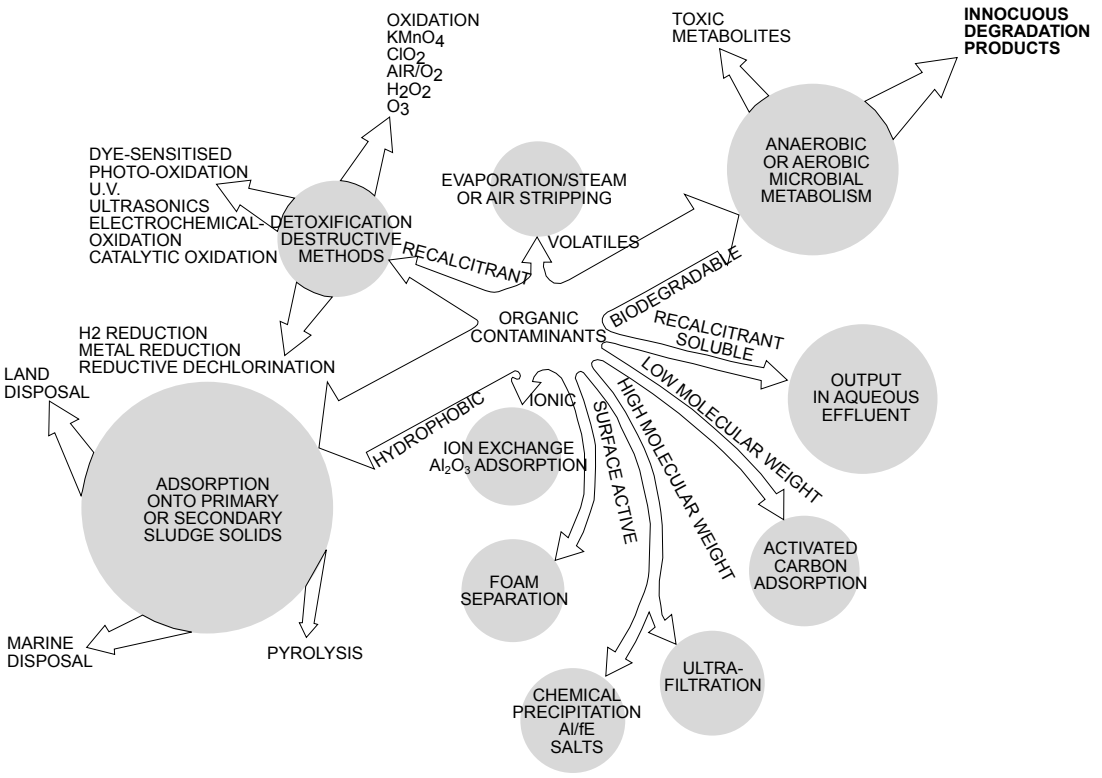


Figure 5.3.: Organic contaminant fate during sewage and industrial effluent treatment adapted from Rogers (1996)

solids and this tendency to accumulate in sewage sludge solids, can be assessed using the octanol - water partition coefficient (K_{ow}). In general the following guide to the significance to sorption can be used:

$logK_{ow}$	$<$	2.5	low sorption potential
$logK_{ow}$	$>$	2.5 and < 4	medium sorption potential
$logK_{ow}$	$>$	4	high sorption potential

The significance of volatilisation losses of specific organic compounds during sewage treatment, can be estimated using the following empirically defined categories, based on Henry's Law constant (H_c) and K_{ow}:

$H_c > 1 \times 10^{-4}$ and $H_c/K_{ow} > 1 \times 10^{-9}$: high volatilisation potential

$H_c < 1 \times 10^{-4}$ and $H_c/K_{ow} < 1 \times 10^{-9}$: low volatilisation potential

Figure 5.4 (from Joss et al. (2006)) gives an overview of kinetic degradation rate constants for 35 PhCs, hormones and personal care products in nutrient-eliminating sludge. According to these data, the load of only four compounds (ibuprofen, paracetamol, 17β-estradiol and estrone) out of 35, are expected to be biological transformed, by more than 90% (k_{biol} >10 L ${g_{ss}}^{-1}$ d^{-1}). Sixteen compounds are expected

to be partially removed ($0.1 > k_{biol} > 10$), whereas no remarkable biological transformation is predicted for 17 compounds ($k_{biol} < 1$; among others most of the macrolide and sulfonamide antibiotics observed). The results of figure 5.4 are generally in good agreement with data found in the literature (Beausse (2004), Buser et al. (1999), Heberer (2002a), Heberer (2002b), Ternes (1998)).

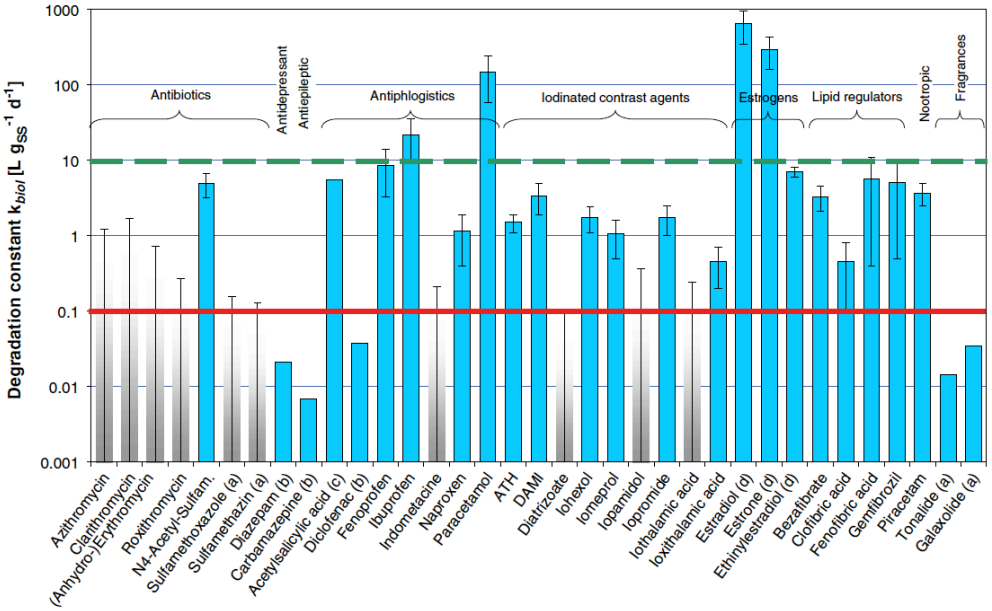


Figure 5.4.: Kinetic degradation constants of 35 pharmaceuticals, hormones and personal care products observed in sludge from nutrient and removing in WWTP

However, some studies differ significantly from our results (diclofenac and indomethacin in Ternes (1998), fenoprofen, ibuprofen, indomethacin, gemfibrozil and estrogens in Urase and Kikuta (2005)): at least part of the difference may be explained by (i) substantially higher experimental pharmaceutical concentration, (ii) sludge origin (sludge age, WW composition, flow scheme) or (iii) sludge handling prior to batch experiments (e.g. artificial substrate dosing, sludge storage).

In figure 5.4 the error bars indicate the 95% confidence interval. The lines at k_{biol} 0.1 and 10 L g_{ss}^{-1} d^{-1} indicate the limits for less than 20% and more than 90% removal expected for nutrient and removing in WWTP. The faded columns indicate values for which the limited experimental resolution allows only identifying an upper limit for k_{biol} (upper error bar).

Stasinakis et al. (2010) explained that investigation of EDCs sorption in batch experiments showed that SRT did not affect the sorption potential of TCS and

BPA, while higher sorption constants were observed for 4-n-nonylphenol at SRT of 20 days. The use of lab-scale continuous-flow systems, showed that for an HRT of 10 h and SRT ranging between 3 and 20 days, the major part of EDCs (>90%) can be removed during activated sludge process, mainly via biodegradation. Calculation of the mean pseudo- first-order biotransformation rates at different SRT showed that EDCs values were ranged between 178 to 507 L g VSS^{-1} $days^{-1}$, 30 to 288 L g VSS^{-1} $days^{-1}$ and 17 to 113 L g VSS^{-1} $days^{-1}$ for 4-n-nonylphenol, triclosan and bisphenol A, respectively.

Resuming the most important removal pathways of organic compounds during WWs treatment are biotransformation - biodegradation, adsorption to the sludge (excess sludge removal) and stripping by aeration (volatilization). Also, abiotic removal from the aqueous phase by hydrolytic degradation and/or isomerisation - epimerisation can occur.

In most of the studies, two processes of abiotic (adsorption) and biotic degradation (transformation by microorganisms) could not be distinguished, and the term *removal* usually refers to a conversion of a certain micropollutant to other compounds than the parent compound. Moreover, without stoichiometric accounting for the human metabolites and products of photo and biodegradation one cannot conclude whether the compound was structurally altered or destroyed, since it could only exist in another state or form.

Sorption of micropollutants onto sludge will mainly depend on two mechanisms (see figure 5.5):

- absorption: hydrophobic interactions of the aliphatic and aromatic groups of a compound with the lipophilic cell membrane of the microorganisms or the lipid fractions of the sludge,
- adsorption: electrostatic interactions of positively charged groups of chemicals with the negatively charged surfaces of microorganisms.

Suspended-growth systems: Limiting factors

The behaviour of micropollutants in suspended biomass in biological systems, which are very common. It is seen that, their biodegradation is tied to a particular pa-

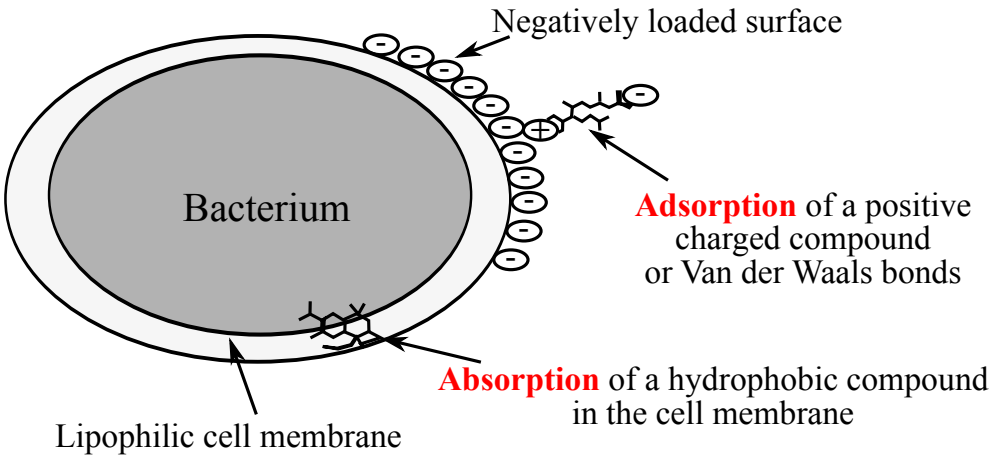


Figure 5.5.: Illustration of adsorption and absorption of pharmaceutical onto the microorganism cell (Larsen et al. (2004))

rameter: the age of the sludge when high (> 20 d) helps the acclimation of many bacterial.

In most WWTP the biological system concerns in a biological treatment, with activated sludge, with sludge age in a range of 5 and 8 days. To increase the micropollutant (like PhCs) removal efficiency may be possible two different strategies: to upgrade the existing plants or to add final treatments (end-of-pipe).

Some compounds may be absorbed or adsorbed into the activated sludge biomas. This is relevant only for those lipophilic and hydrophilic compounds that can interact specifically (such as surfactants) with the staple of activated sludge. In these cases, those compounds *captured* from the flakes of activated sludge, partially degraded inside sludge floc bacteria, some remain in the settled sludge and then passed to subsequent stages of treatment sludge.

In the case of CAS systems, the effluent of the secondary settler is subject to variations in the content of suspended solids, to the inevitable leakage of the activated sludge tank. Consequently, even as it was adsorbed / antigen is not retained. MBR system guarantees a constant high quality final effluent for the most efficient removal of suspended solids (often < 1 mg L^{-1}). The difficulty at this point is to identify classes of compounds that are not adsorbed by activated sludge and, because of their chemical and physical - remain dissolved in water and are difficult to degrade, such as certain medications such as carbamazepine, diclofenac, contrast media. Some of the most recent published studies analysed, with regard to the removal of these mi-

cronquinanti, the succession of different steps of advanced treatments downstream of activated sludge biological systems (Okuda et al. (2008), Suarez et al. (2008)).

5.1.3. MBR

There is a lot to admire about membrane bioreactors (MBRs). This emerging WWs treatment technology combines a suspended growth biomass, similar to those used in the traditional activated sludge process, with a membrane system that replaces gravity sedimentation and that retains biomass and clarifies effluent (Stephenson et al. (2000)). MBRs offer a host of technical advantages over activated sludge systems, such as small size, and seem to be well suited for applications such as water reuse. Figure 5.6 illustrates the components of an MBR and contrasts them, with those of a traditional activated sludge process, as reported for example in Daigger et al. (2005).

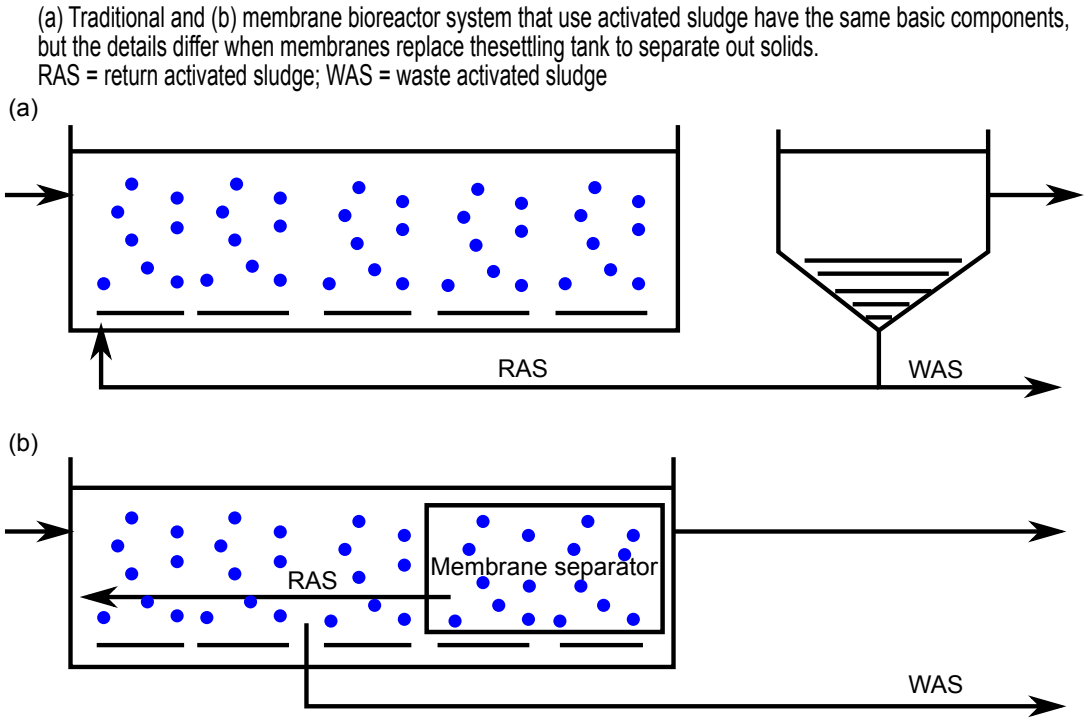


Figure 5.6.: Comparison of traditional and bioreactor methods (from Daigger et al. (2005))

One of the key issues in wastewater recycling is the emerging problem of micropollutants such as pharmaceuticals, hormones, fragrances and personal care products (PCPs).

The MBR technology integrates biological degradation of organic matter present in wastewater with membrane filtration, thus surpassing the limitations of the conventional activated sludge (CAS) treatment (e.g., limited operational solids retention time (SRT), sludge settling characteristics). At prolonged SRT applied in an MBR the biomass growth is not restricted to fast-growing and floc-forming microorganisms, whereas the dispersed bacteria can develop.

The fate of a certain pharmaceutical in a complex system of WWTP will depend on various parameters (e.g., applied SRT, hydraulic retention time (HRT), temperature, pH, biomass concentration, compound's polarity, biodegradability, cation-exchange properties). During sewage treatment pharmaceutical residues can be removed from the aqueous phase either through abiotic processes (e.g., sorption isomerisation or epimerisation, hydrolytic degradation) or by biotic transformation or degradation.

However, PhCs can absorb onto bacterial lipid structure and fat fraction of the sewage sludge through hydrophobic interactions (e.g., aliphatic and aromatic groups), adsorb onto often negatively charged polysaccharide structures on the outside of bacterial cells through electrostatic interactions (e.g., amino groups), and or they can bind chemically to bacterial proteins and nucleic acids (Meakins et al. (1994)).

Some authors tried to estimate separately contributions of adsorption and biodegradation to the removal of PhCs in CAS and MBR treatments based on literature values for solid-water distribution coefficients (K_d) or by direct measurements of the adsorbed and dissolved amounts of pharmaceuticals in batch experiments (Kimura et al. (2007), Clara et al. (2005a), Joss et al. (2006), Urase and Kikuta (2005)).

In genearal MBR technology generally outperforms the CAS treatment in removing PhCs from WWs (Radjenovic et al. (2009)).

As reported for example in Radjenovic et al. (2009), the elimination of some compounds that showed recalcitrant for the CAS treatment was significantly improved in the MBRs up to around from 32 to 65% (figure 5.7).

From the aspect of the excess sludge produced, advanced MBR technology would be attractive concept, not only in terms of the cost reduction of sludge treatment due to its lowered production, but also because it diminishes the environmental impact of WWs treatment, since the MBR sludge is less contaminated with PhCs than the

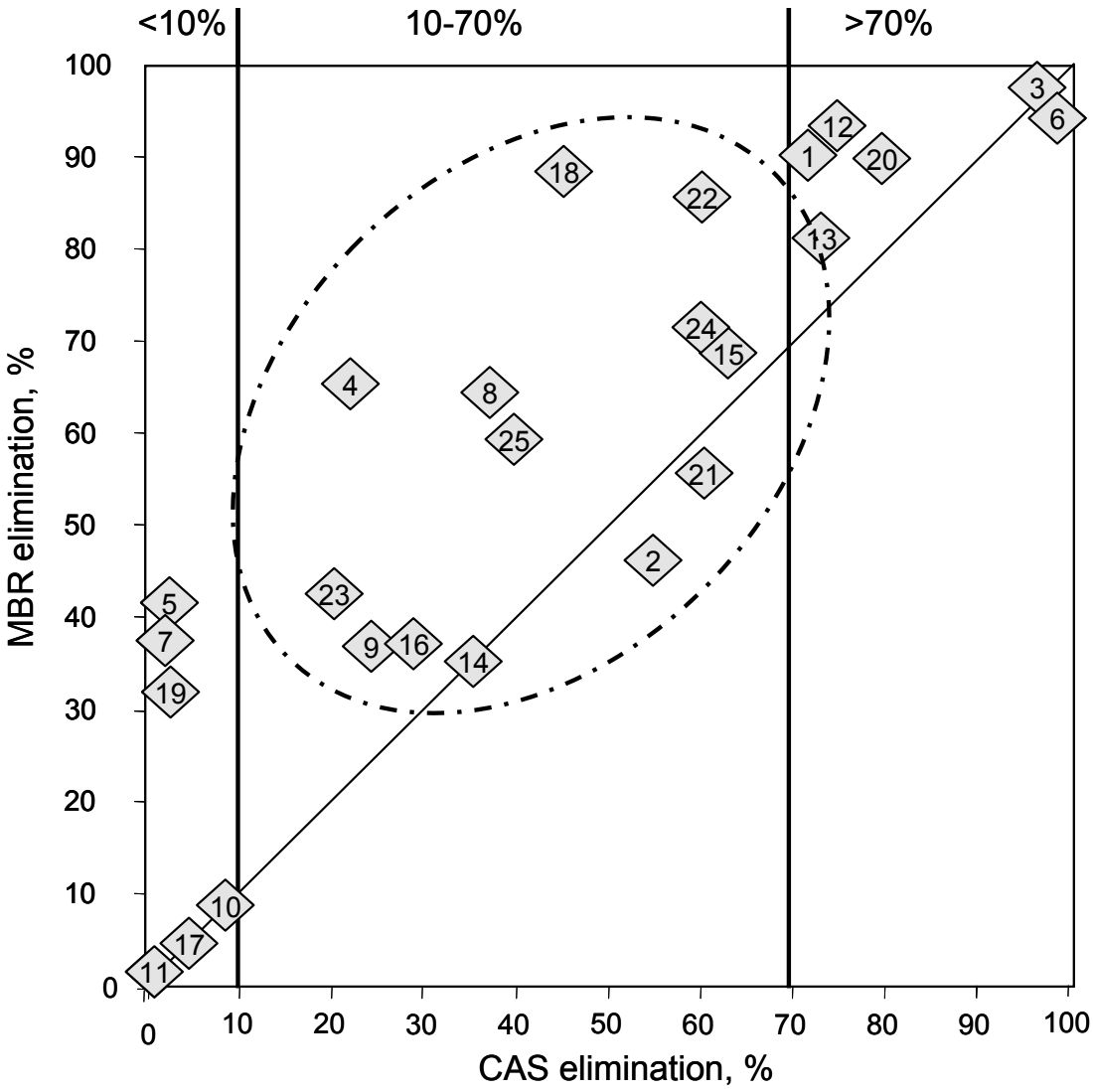


Figure 5.7.: Comparison of the mean removals of encountered pharmaceuticals in full-scale CAS and pilot-scale MBRs. From Radjenovic et al. (2009)

sludge produced during the conventional treatment. The amount of PhCs, sorbed onto sewage sludge may increase the environmental risk of these micropollutants, since they can become bioavailable when conditions for desorption are created.

Moreover the literature in Bouju et al. (2008) shows that MBRs should be more efficient on Persistent organic pollutants (POPs) removal than CAS, especially on the substances which are poorly biodegradable, while it does not improve the removal efficiency for the non-degradable ones. The comparison with the removal obtained in a very large conventional WWTP operating at quite high SRT will be particularly significant.

Also Hawkshead (2008) concludes that MBR system can represent an important alternative to CA in the HWWs treatments and, for a correct treatment of HWWs, Beier et al. (2011) reports the design requirements for MBRs. Based on the operational experience gained at this site and on technical and economic optimisation, the following aspects should be considered in the design of MBR treating hospital wastewaters in high density urban areas:

- separate rainwater collection to reduce dilution effects
- where applicable, separation of water streams with low pharmaceutical concentrations (e.g. kitchen and laundry wastewaters)
- sludge age in the MBR $>$ 100 days to allow for biomass adaptation
- thermal treatment of the waste activated sludge and screenings for complete destruction of the adsorbed pharmaceuticals
- consideration of the special requirements on emission levels (noise and aerosols) for hospital patients with a weak immune system and/or needing a quiet environment as well as those of nearby residents.

Also Liu et al. (2010) think that membrane technology is more efficient at removing pathological microorganism, compared with other WW treatment systems.

Recently, more attention has been paid to the membrane bioreactor (MBR) technology for HWWs treatment, because of its higher efficiency in pollutant removal, excellent effluent quality, low/ zero sludge production, compact size and lower energy consumption (Stephenson et al. (2000),). Previous researches on MBRs have

shown that an MBR is extremely efficient in the removal of bacteria (Krauth and Staab (1993)) and viruses (Lv et al. (2006)).

5.1.4. Nanofiltration

The removal of PhCs by NF membranes occurs via a combination of three mechanisms: adsorption, sieving and electrostatic repulsion. The removal efficiency can be very different and varied from compound to compound and it is strictly correlated to:

- micropollutants physical-chemical properties like molecular size, solubility, diffusivity, polarity, hydrophobicity and charge,
- membrane properties like permeability, pore size, hydrophobicity and surface charge
- membrane operating conditions like flux, transmembrane pressure, rejections or recovery and water feed quality.

NF has been demonstrated to be a promising alternative for eliminating PhCs, as it is able to achieve removal rates greater than 90%, as reported for example in Yoon et al. (2006) and Bolong et al. (2009).

It is also important to consider RO and NF brine disposal. In general, brine is much more toxic than the influent water, so it is not sustainable to dispose of it into natural water as reported by Watkinson et al. (2007).

Beier et al. (2010) conclude his comparison between NF and RO, explaining that in general MBR technology and downstream high pressure membrane filtration is an adequate approach for the specific treatment of hot spot wastewater with hight concentrations of trace pollutant or PhCs residues. In particular only RO ensured an entire removal of relevant PhCs residues from HWWs. Nonetheless, RO has some major disadvantages particularly due to the limited yield and the retentates which need to be adequately disposed. However, the appropriateness of an application of NF/RO should be checked for each individual case.

5.1.5. Reverse osmosis

Several studies describes the effectiveness of RO in the removal of PPCPs and endocrine disrupter compounds from secondary wastewater effluents (among them Snyder et al. (2003), Oppenheimer et al. (2007)). Braghetta and Brownawell (2002) estimated removals of many compounds to be greater than 90%. Lower removal rates were found for diclofenac (55.2-60%) and ketoprofen (64.3%). According to WERF (2005), RO achieved removal rates of 90% or better for naturally occurring and synthetic steroids, organohalides and other compounds. Oppenheimer et al. (2007) found that RO was able to remove all the investigated compounds below their corresponding detection limits, including those that were not significantly removed at SRTs of 30 days (for instance, galaxolide) using CAS treatment or media filtration.

Beier et al. (2010) show that only RO ensured an entire removal of relevant pharmaceutical residues from HWWs.

5.1.6. Chlorination

Ternes et al. (2003), and Huber et al. (2005) demonstrated that the ozone amounts required for PPCPs oxidation lead to a partial disinfection. It is expected that, as for sorbed compounds, microorganisms incorporated into particulate matter, would be significantly shielded from ozone or $OH^{\cdot}$ radicals. A concentration of 5-10 mg O_3 L^{-1} and a contact time of 15-20 min are sufficient to obtain a reduction of 2-3 log units (Chiang et al. (2003); Ternes and Joss (2006)). Referring to the disinfection action of chlorine and its compounds, Nardi et al. (1995) found a good removal rate of bacteria as well as viruses in the effluent from an infectious diseases ward by adding 10 mg L^{-1} of ClO_2 and guaranteeing a contact time of 30 mins. Emmanuel (2004) studied the toxicological effects of disinfection using NaClO. He found that doses of 1-8 mg L^{-1} of disinfectants can greatly reduce bacteria pollution but give rise to toxicity effects on aquatic organisms, thereby contributing to the formation of AOX in HWWs.

For our studies about the disinfection with PAA and NaClO of raw HWWs see section 4.1 where are reported all the results and some comments about this practice.

5.1.7. Ozonation and AOPs

These techniques are promising for an efficient degradation of pharmaceuticals in water and wastewaters (Chiang et al. (2003); Huber et al. (2003); Balcioglu and Otker (2003); Ternes et al. (2003); Andreozzi et al. (2005); Machado et al. (2007); Zimmermann et al. (2008)). A common result is an increment in the ratio BOD_5/COD and the improvement in the biodegradability of persistent substances such as antibiotics, cytostatic agents, hormones, X-ray contrast media, carbamazepine and some acidic drugs like clofibric acid. Some pharmaceuticals are extremely reactive towards molecular ozone: some antibiotics, the anticonvulsant carbamazepine, the antinflammatory diclofenac, the estrogen 17β-estradiol. Others are relatively resistant to ozonation: the anti-anxiety agent diazepam, the analgesic ibuprofen. ICM are in general particularly refractory to ozonation.

Ozone-base AOPs (O_3/H_2O_2, O_3/UV), Fenton-type processes and photochemical AOPs are generally more effective than ozonation alone due to enhanced generation of hydroxyl radicals and photon-initiated cleavage of carbon-halogen bonds, thus they are recommended for the treatment of these recalcitrant substances (Ikehata et al. (2006)).

The degree of degradation of PhCs achieved by ozonation or AOPs depends on a number of factors: oxidant dose, concentration of pharmaceuticals, wastewater quality parameters, mode of operation.

The dose of ozone that is commonly applied ranges between 5-15 mg L^{-1} depending on the COD in the wastewaters, and a contact time of about 15-30 min (Ternes et al. (2003); Ternes and Joss (2006)). The removal of PhCs is in general $> 90\%$. The presence of particulate matter at concentrations regularly present in the secondary effluent does not influence the removal efficiency of soluble compounds showing high reaction rates with ozone. Huber et al. (2005) show that soluble compounds readily reacting with ozone, will be oxidized a hundred times faster than organic matter agglomerated particles due to limitation by diffusion. However, the removal efficiency of compounds requiring higher ozone dosage is reduced with increasing content of organic particulate matter due to the loss of oxidant equivalents.

AOPs can be more effective than ozonation for many compounds, but for others, like ICMs or complex molecule compounds containing chlorines, they lead to a slight

increase of oxidation efficiency (Joss et al. (2004); Wen et al. (2004); Pauwels and Verstraete (2006); Bouju et al. (2008)), thus further studies are necessary.

Ternes et al. (2003) reports that Ozonation using 5-15 mg L^{-1} of ozone is appropriate to oxidize pharmaceuticals, musk fragrances, estrogens and to simultaneously inactivate relevant microorganisms.

The results presented in Huber et al. (2005) have shown that important classes of pharmaceuticals present in WWs effluents such as macrolide and sulfonamide antibiotics as well as synthetic and natural estrogens, can be selectively oxidized by use of relatively low O_3 doses. Furthermore, the results demonstrated that suspended solids have only a minor effect on the oxidation of pharmaceuticals. Ozonation of wastewater effluents will mainly be a viable solution when the treatment objectives include micropollutant oxidation and disinfection. Though suspended solids have limited effect on micropollutant oxidation, they have a clearly negative impact on disinfection as shown in ref 36 and indicated by the inactivation data for *E. coli* in the present study. In the regular CAS effluent, an O_3 dosage of 5 mg L^{-1} seems sufficient to achieve the guideline values (100 fecal coliforms/100 mL) set by the EU bathing water quality directive.

5.1.8. Natural polishing treatment

Works about natural treatments are not quite diffuse and in general the authors are:: Golet et al. (2003), Clara et al. (2004), Clara et al. (2005a), Lindqvist et al. (2005), Brown et al. (2006), Lindberg et al. (2006), Lishman et al. (2006), Nakada et al. (2006), Yu et al. (2006), Gomez et al. (2007), Kim and Aga (2007), Kimura et al. (2007), Santos et al. (2007), Vieno et al. (2007a), Watkinson et al. (2007), Choi et al. (2008), Gulkowska et al. (2008), Kasprzyk-Hordern et al. (2009), Matamoros et al. (2009), Santos et al. (2009), Zhou et al. (2009), Rosal et al. (2010).

CWs can promote removal of PhCs through a number of different mechanisms, including photolysis, plant uptake, microbial degradation and sorption to the soil (White et al. (2006), Matamoros et al. (2005), Matamoros et al. (2008)). The main benefits of horizontal and vertical subsurface flow systems are the existence of aerobic, anaerobic and anoxic conditions in proximity to the plant rhizomes which provide an opportunity to reduce concentrations of different drug compounds, as

some pharmaceuticals are best reduced under aerobic conditions (ibuprofen), removal of others is favored by anaerobic conditions (clofibric acid, diclofenac) (Lin and Reinhard (2005)) and halogenated pollutants are eliminated at a higher rate in anoxic conditions. Experimental studies conducted by Matamoros et al. (2008) and Zwiener and Frimmel (2003) showed that aerobic conditions are in general more efficient in removing most emerging contaminants than anerobic pathways. In addition, the photodegradation processes, which take place in surface flow systems, are able to eliminate certain PPCPs (like ketroprofene and diclofenac) from aquatic environments (Andreozzi et al. (2003), Bartels and von Tumpling (2008), Zhou et al. (2009)). High hydraulic retention times promote biodegradation and photodegradation reactions involved in the removal of emerging contaminants.

Compact biofilters, biological sand filters and constructed wetlands are feasible technologies to remove a broad spectrum of contaminants including PPCPs from UWWs in sparsely populated areas. Further research on household WWs treatment systems is, however, still required to fully confirm these results as reported in Matamoros et al. (2009).

Matamoros et al. (2008) explain that the higher removal efficiencies for emerging micro contaminants observed in his study than those reported for H-SSF CW and conventional WWTPs seem to be related to the high HRT (i.e. 1 month in his study). This high HRT promotes biodegradation and photodegradation reactions that are involved in the removal of emerging contaminants. Furthermore, seasonal and spatial trends showed a high dependence on temperature (biodegradation) and sun irradiation (photodegradation) for the moderately removed compounds. Apparent distribution constants K_d are strongly dependant on the compound ionization. On the other hand, the neutral compounds are correlated to their hydrophobicity ($\log K_{ow}$). In general, the studied wetland has a good capacity for removing a variety of emerging contaminants, close to the ones obtained in highcost tertiary treatments (ozonation or MBR). Therefore, the application of cost-effective technologies such as CWs should be considered as an efficient alternative for reducing the amount of emerging contaminants discharged into aquatic ecosystems.

Moreover Park et al. (2009) studied an engineered CW connected to both a WWTP and a river with respect to removal potential and related mechanisms for 9

different organic micropollutants, including PhCs, EDCs and personal care products. Fairly good removal trends were shown for atenolol, naproxen and triclosan. Sulfamethoxazole and dilantine, and carbamazepine, diazepam and triclosan exhibited medium-range and fluctuating (or somewhat low) removal behaviors, respectively. Attempts were made to determine the dominant removal mechanisms for tested micropollutants extracted from wetlands soils and plants, using micropollutant extraction methods and two parameters (i.e., $\log K_{ow}$ and pKa); however, no distinct patterns were found. Hence, the results of Park et al. (2009) suggest the necessity for further investigations into the removal mechanisms of micropollutants via biodegradation under anoxic conditions.

Biodegradation, plant exudates and uptake, sedimentation and sorption onto filling media are the main elimination pathways. Many attempts have been made to find some relationship between the physicochemical characteristics of PhCs (octanol water partition coefficient K_{ow}, Henry's constant H, water solubility Sw, vapour pressure Pv, organic carbon partition coefficient K_{oc}, acid dissociation constant Ka) and their fate in constructed wetland systems (Imfeld et al. (2009), Kummerer (2009), Park et al. (2009)), but no clear correlation has yet been found due to the great variability of compounds and their behaviour. Thus, graphs plotting the percentage removal rate vs. molecular weight or vs. $\log K_{ow}$ yield clouds of data, showing a wide variability in the behaviour of the substances considered.

For instance, some pharmaceuticals contain planar aromatic structures, which favour intercalation, for example into the layers of some clay minerals. Therefore, the sorption of such compounds depends not only on the $\log K_{ow}$, which is the lipophilicity of the sorbed molecule, but is also governed by pH, redox potential, stereochemical structure and the chemical nature of both the sorbent and the sorbed molecule (Kummerer (2009)).

The coexistence of several microenvironments in CWs allows both the thermodynamic feasibility of chemical reactions and the development of a great variety of microbiological communities able to guarantee the enzymatic capacity necessary to achieve the target biogeochemical reactions. This favours various metabolic pathways and therefore leads to PhC degradation.

This microenvironmental coexistence is due to the variation of physicochemical

parameters on different gradients inside the CWs (D'Angelo (2002), Dusek et al. (2008), Imfeld et al. (2009)), some of which may be generated by the organisms inhabiting the CW, or by the presence of ramified roots within the medium. These tend to create aerobic zones near anoxic or anaerobic ones (Stottmeister et al. (2003), Imfeld et al. (2009)), establishing dynamic oxic or anoxic interfaces in wetlands as a result of water level fluctuations, oxygen diffusion or advection through the water column and filling medium, and active oxygen transport through the rhizosphere via plant tissues.

Summer conditions (mainly warmth and plant activity), high redox potential (anoxic and oxic conditions) promote the removal of PhCs (Hijosa-Valsero et al. (2010b)). It also seems that anoxic conditions favour the biodegradation of micropollutants as they promote biogeochemical reactions: for example, the biological transformation of amide and urea functional groups (attached to atenolol, carbamazepine, dilantin) via mediated hydrolysis reactions has been documented (Chisaka and Kearney (1970), Englehardt et al. (1973), Matamoros et al. (2008)).

However, aerobic transformations are generally faster than anaerobic ones for low-chlorinated compounds, while for polyhalogenated compounds aerobic degradation rates are slower. Furthermore, highly chlorinated substances, like diclofenac, are known to be biodegraded via a microbe-mediated reduction (Mohn and Tiedje (1992), Schwarzenbach et al. (2003), Matamoros et al. (2007b), Matamoros et al. (2008)). These compounds, characterized by their low water solubility, become more soluble, and therefore more bioavailable, after some initial reductive dechlorination steps. Under anaerobic conditions, however, microbial degradation takes time and a subsequent aerobic degradation step is necessary for breaking down the remaining carbon skeleton.

According to Jones et al. (2005a), long and highly branched side chains render a compound more persistent, whereas unsaturated aliphatic compounds are more biodegradable than saturated or aromatic ones featuring complex ring structures and sulphate or halogen groups.

Occasionally, release of pharmaceuticals occurred in natural systems. It could be attributable to the presence of substances, e.g. human metabolites, in the inflow to the treatment step. These could subsequently be transformed into the investigated

PhC during treatment, as in the case of sulfadiazine and sulfamethoxazole (Gobel et al. (2005). It is also possible that the PhC was hidden among the suspended particles in the influent and later released into the water column during its passage through the filling medium. Indeed, carbamazepine, as already noted, is one of the most recalcitrant PhCs due to its high hydrophobicity ($\log K_{ow}$ is 3.5) and refractory behaviour. Its main elimination mechanism is by retention and adsorption onto the organic surfaces available in the CW. It is possible that when sorption - desorption equilibrium is reached, the contaminant will be *reversibly* retained and then released into the water column.

The removal mechanisms include abiotic and biotic pathways: sorption onto sediments and gravel and biodegradation. They depend on many aspects: in particular H-SSF bed conditions (redox conditions, pH and temperature) chemical characteristics of the wastewater (COD and N compounds), chemical properties of the pharmaceuticals (Log Kow, pka, logkd).

5.1.9. Photodegradation

Generally speaking, both abiotic and biotic processes determine the fate of organic compounds in the aquatic environment. For any pollutant, including PhCs, abiotic transformations in surface waters may occur via hydrolysis and photolysis. Pharmaceuticals, usually designed for oral intake, are as a rule resistant to hydrolysis suggesting the mechanism of direct and indirect photolysis as a primary pathway for their abiotic transformation in surface waters. While direct photolysis of chemical species is caused by direct absorption of solar light (Zepp and Cline (1977)), the indirect photolysis involves natural photosensitizers like nitrate and humic acids. Under solar irradiation, these naturally occurring constituents can generate strong oxidant species such as hydroxyl radicals and singlet oxygen (Zepp et al. (1981)).

On the other hand, humic acids absorbing solar radiation (Gao and Zepp (1998)) may, by inner filtering, reduce the rate of photodegradation of other organic species present in the aquatic environment. An additional factor that strongly influences the rate of photodegradation for any particular pharmaceutical present in the surface waters, is the variation in the intensity of solar irradiance with both latitude and season. For a given latitude and the season, the spectral solar irradiance can be

measured experimentally using pyranometer or can be found in specialized literature (Frank and Klopffer (1988); EPA (1996)).

STP effluents from four European countries (France, Italy, Greece and Sweden) with no previous record of pollutants of this type, have been analyzed for the presence of pharmaceutical residues. The analyses were performed using GC-MS and HPLC-MS/MS procedures developed in this study. More than 20 individual pharmaceuticals belonging to different therapeutic classes have been found. Antibiotics, gemfibrozil, ibuprofen, naproxen, carbamazepine and the majority of b-blockers have been detected in all samples. The presence of ofloxacin, lomefloxacin, enoxacin and flurbiprofen found in this study has not previously been reported in STP effluents. In contrast to data published for Germany, betaxolol was not detected in any of the investigated STP effluents, while trimetoprim and sulfamethoxazole were present in much lower concentrations than reported for the effluents from German STPs. The persistence to abiotic photodegradation has been evaluated for six selected pharmaceuticals among those found in the STP effluents. Quantum yields for photodegradation in salt- and organic-free water estimated for carbamazepine, diclofenac, clofibric acid, sulphamethoxazole, oflaxocin and propranolol have been used to predict half-life times at varying seasons and latitudes. The results demonstrate that the photodegradation halflife times of carbamazepine and clofibric acid are approaching 100 days in winter at the highest latitudes (50 N), whereas under the same conditions sulfamethoxazole, diclofenac, ofloxacin and propranolol undergo much faster degradations with $t_{1/2}$ respectively of 2.4, 5.0, 10.6 and 16.8 days. The presence of nitrate ions in aqueous solutions (5.0-15.0 mg L^{-1}) results in a reduction of $t_{1/2}$ for the studied compounds, propranolol excepted. Humic acids (concentration of 5.0 mg L^{-1}) act as inner filters during the photodegradation of carbamazepine and diclofenac and as photosensitizers for sulphamethoxazole, clofibric acid, oflaxocin and propranolol Andreozzi et al. (2003).

The data strongly suggest inputs of diclofenac into rivers and lakes from human medical use viaWWTPs. The study of Buser et al. (1998), however, also showed that diclofenac is not very persistent in a lake (Greifensee) and that it is rapidly degraded, most likely via direct photolysis. The results are important because they document the rapid elimination of this compound in surface water under field conditions. The

findings have transfer character because the same process can be expected in other water bodies (lakes, streams) with a sufficient time constant, as suggested by the consistently low concentrations observed in the outflows of other lakes. This rapid elimination of diclofenac in the lake is different from the behavior of many other environmental contaminants. So far, the evidence for photodegradation is from laboratory experiments and kinetic considerations. Direct evidence, such as from photodegradation products in the lake, is still lacking and additional research is required for verification.

5.2. Role of pH and Redox potential

Many pharmaceuticals have weak acid or weak base functional group as part of their structure that lead to thermodynamically accessible ionized and unionized forms at physiological pH values. The ionized forms aid aqueous solubility, while the non-ionized forms can diffuse more easily through lipophilic membranes. Consequently, numerous pharmaceuticals have environmentally relevant pK_a values, with ionized and non-ionized species, being present under natural conditions. Each of these species must be considered to fully anticipate the pharmaceutical's aquatic chemical behaviour. This situation is exemplified by a set of sulfa drugs, whose photochemistry is strongly modulated by their speciation. The effect of speciation of photochemical reaction rate applies not only to direct processes, but also to indirect processes. For example, it is well documented, that single oxygen reacts quickly with phenolate ions, but not with phenols (Petrovic and Barcelo (2007)).

Kummerer (2009) explains that antibiotics can be grouped by either their chemical structure or mechanism of action. They are a diverse group of chemicals, that can be divided into different sub-groups such as β-lactams, quinolones, tetracyclines, macrolides, sulphonamides and others. They are often complex molecules which may possess different functionalities within the same molecule. Therefore, under different pH conditions antibiotics can be neutral, cationic, anionic, or zwitterionic (figure 5.8a and b and figure 5.9a and b). Because of the different functionalities within a single molecule, their physico-chemical and biological properties such as $\log P_{ow}$, sorption behavior, photo reactivity and antibiotic activity and toxicty may

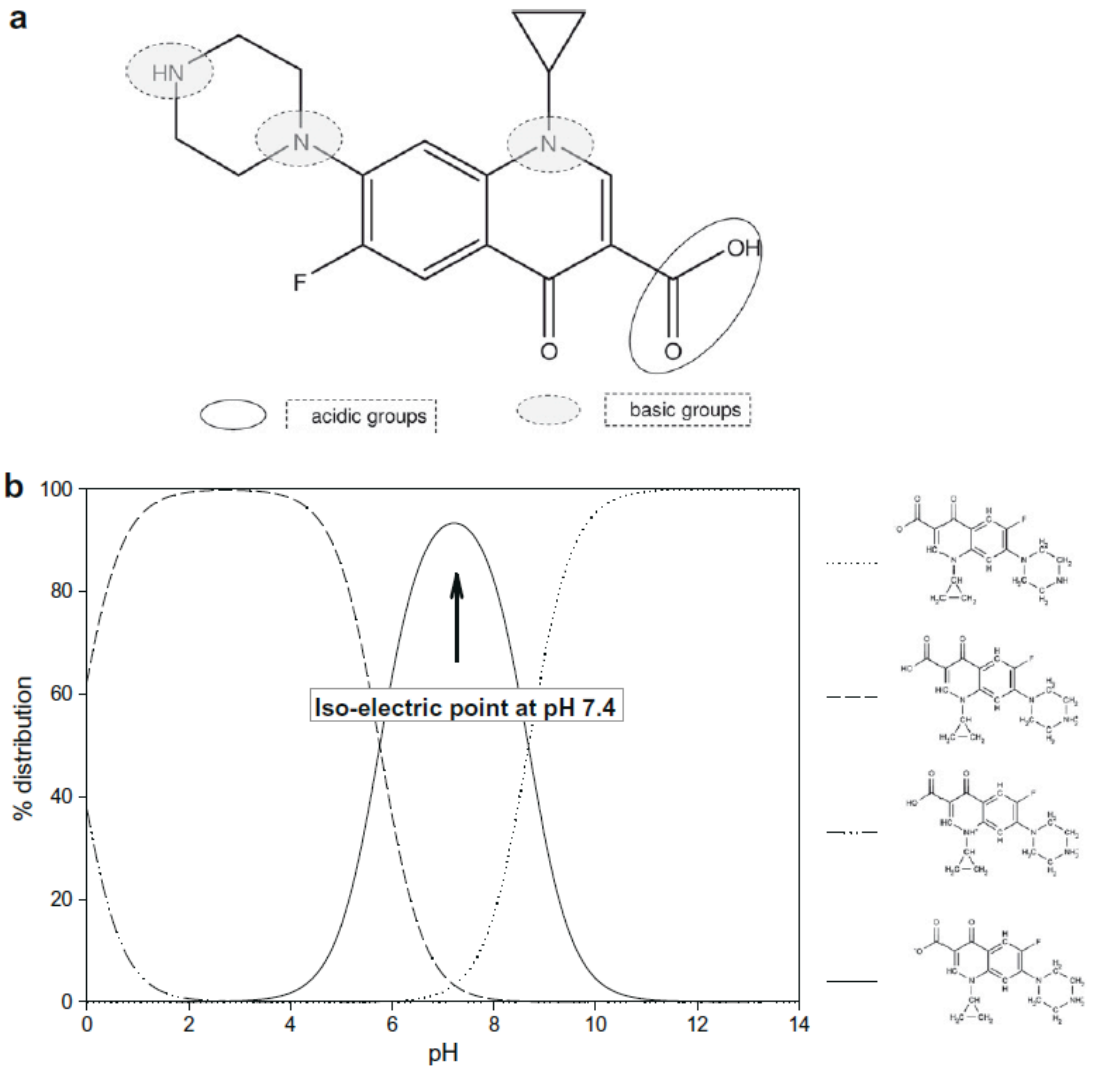


Figure 5.8.: Chemical structure of ciprofloxacin (a); at different pH ciprofloxacin carries different electrical charges i.e., different chemical species are present (b). From Kummerer (2009)

change with pH.

Ciprofloxacin (figure 5.8a), for example, possesses both basic and acidic functionalities. The acid constants are 6.16 and 8.63. At a pH of 7.4, the iso-electric point of ciprofloxacin, the molecule carries both a negative and a positive charge, i.e. it is neutral as an entity despite these charges within the molecule (figure 5.9b). Solubility, hydrophobictiy and hydrophilicity, and therefore $\log K_{ow}$ or the distribution coefficient $\log K_D$, are all dependant upon pH.

Suarez et al. (2010) conclude that the main removal mechanisms for PPCPs only (bio)transformation were significant for the majority of compounds. In the case of musk fragrances, a significant fraction (7-18%) of compounds left the anoxic

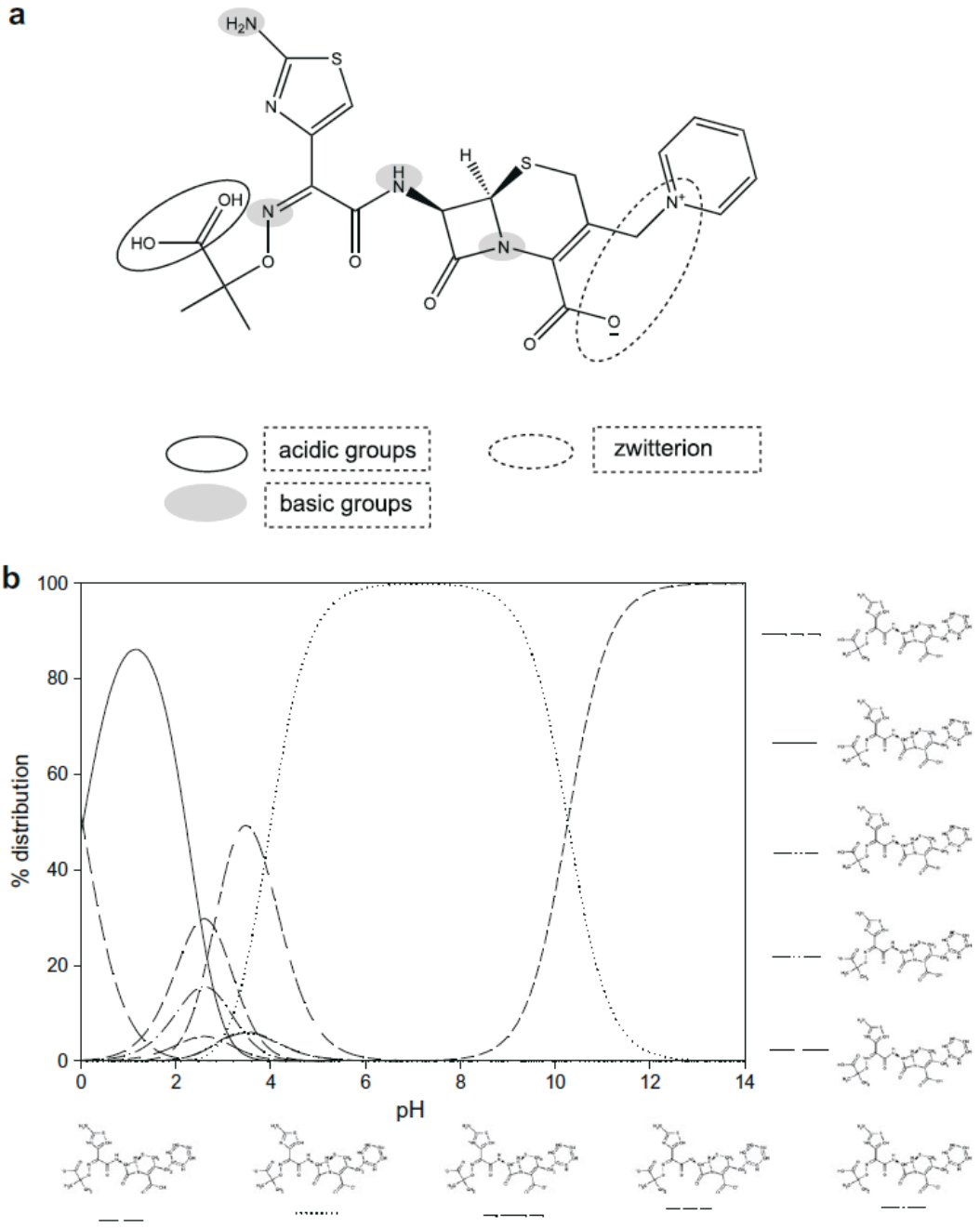


Figure 5.9.: Chemical structure of ceftazidime (a); ceftazidime forms an internal zwitterion and can from additional chemical species as a function of pH (b). From Kummerer (2009)

reactor sorbed onto solids, whereas sorption was negligible in the case of the aerobic plant, which was associated to the better settling characteristics of the nitrifying biomass developed in that reactor. Volatilisation was only significant for ADBI and contributed between 3 and 16% to the removal of this substance in the aerobic system.

5.3. Source separations

In an interesting article Ternes et al. (2004b) explained that many PPCPs have limited biological degradability. Therefore, these compounds are only partially eliminated when passing through WWTPs and end up in receiving waters or sorbed to sludge that may be used for fertilizer. Source control and apportionment appear to be the permanent, cost-effective solution for most compounds.

In particular:

- Separate treatment of HWWs. HWWs is heavily loaded with pharmaceuticals and antibiotic-resistant bacteria. Separate treatment of HWWs, such as by using a membrane bioreactor followed by ozonation of the effluent, should be considered. These measures could also be beneficial to the hospital. Treated wastewater could be reused for flushing toilets and for gardening or it could be directly discharged, reducing associated drinking-water fees and avoiding wastewater fees.

- Labeling of PPCPs. Adding information about the environmental impacts of a PPCP to its packaging could significantly reduce the use of harmful chemicals. For instance, Sweden has discussed introducing an environmental label for pharmaceuticals, in cooperation with the chemical industry. This would enable physicians and patients to select the most environmentally friendly pharmaceuticals for a particular course of treatment (Ternes et al. (2004b)).

- Disposal of PPCPs. The disposal of PPCPs should be controlled and supervised. For example, as general practice, expired or superfluous products should be collected and incinerated or possibly reused under controlled conditions.

- Urine separation. Pharmaceuticals are excreted to a great extent in urine

as reported in Ternes et al. (2003). Larsen and Gujer (1996) shown that separation and unique treatment of urine would significantly reduce the loading of the wastewater and would allow recycling of the nutrients.

However, these four measures require political decisions, acceptance from the general population, money for new infrastructure, and decades for their implementation. Therefore, in the short term, a load reduction is easier to achieve within the WWTP.

Lienert et al. (2007a) concludes that the assumption that most pharmaceuticals are excreted with urine could be verified to a certain extent. This statement is valid for some pharmaceuticals and therapeutic groups, but is not all true for others. Some of the detected inconsistency reflects biologically variability, but much is caused by the large difference in physicochemical proprieties of the pharmaceuticals. Moreover, just relying on mass balance does not necessarily correspond with the ecotoxicological relevance.

In substance 70% of a pharmaceuticals was excreted via urine but Lienert et al. (2007b) found that the environmental risk potential was estimated to be about equal in urine and faeces. However they hypothesise that the PhCs in faeces, wich are generally more lipophilic, might adsorb well to faecal matter and end up in the sludge. If this is true, the fraction of micropollutants in faeces might be better removable from WWs than the hydrophilic fraction in urine and a combination of the two measures might prove to be very effective.

A solution for the final reduction of the PhCs diffusion into the environment is for example the incineration. More countries, like for example Switzerland, use this practice for the sludge deriving from WWTP.

5.4. Sustainable Technologies for HWWs

Essentially, hospitals are the main source of pharmaceutical compounds (PhCs) released into the environment. Generally, their discharges are co-treated with UWWs, resulting in a decrement of the recalcitrant compounds concentrations in the final effluent due to water dilution. However, as many PhCs resist normal treatments, pollutant load does not change.

HWWs are composed of the effluents of three different services: (i) general services

(kitchen, internal laundry, heating and cooling systems), (ii) diagnostic services (laboratories, radiology departments, outpatients' departments, transfusion centres) and (iii) wards (general medicine, surgery, specialities, haemodialysis, etc.). In Italy and in many other countries, by law, the effluents from specific wards or services (such as nuclear medicine or histological laboratories) that contain radioactive wastes or anatomical parts cannot be discharged into the hospital sewage network, but must be collected in adequate hermetic baskets and given to authorized disposal firms (Emilia-Romagna (2009)).

By law, HWWs are often considered to be of the same pollutant nature as UWWs, and so they are generally discharged into (municipal) sewer networks, collected at a WWTP and treated along with UWWs. The only pre-treatment that could be required before entering the sewer is a mild chlorination of the whole effluent in order to reduce its microbiological load.

WWTPs were originally built, and have more recently been upgraded, with the aim of removing carbon, nitrogen and phosphorus compounds in addition to the microbiological organisms which are the pollutants regularly arriving at the plant in concentrations to the order of mg L^{-1} and at least 10^5 CFU/100 mL. HWWs represent a unique kind of wastewater due to the nature and quantity of the micropollutants which are typically present at μg L^{-1}: active substances of medicines and their metabolites, chemicals, heavy metals, disinfectants and sterilizers, radioactive markers, (Emmanuel et al. (2001); Kummerer (2001); Altin et al. (2003); Jones et al. (2005a)). Moreover, HWW flow rates generally amount to only a small percentage of the total influent flow rate for co-treatment at a municipal WWTP. Consequently, dilution of HWWs with UWWs usually results in a decrement of the PhCs content in the final effluent (from μg L^{-1} to ng L^{-1}), but not in the total load, that is, the quantity released daily into the receiving water body.

In cases where the hospital component represents a significant percentage (> 25%) of the WWs entering to the WWTP, and the receiving water, is intended for irrigation or recreational uses, it would be take in consideration a good treatment with chemical and biological degradation and separation, such as MBR, ozonation, advanced oxidation systems.

The ability to degrade the more persistent substances depends on the availability

of a sufficient number of specific microorganisms and their time of acclimatization. Sufficiently high sludge age (at least 25-30 d) promote the occurrence of these conditions, even if they are not always sufficient to complete degradation (Joss et al. (2004)).

Some PhCs, as well as bacteria and viruses, tend to adsorb or absorbed on the surface of solids within the biological reactor. Filtration through a UF membrane due to the small pore size that characterizes this technology, can effectively stop all the non solved contaminants. Therefore, the MBR system with UF membranes are a suitable technology for the HWWs treatments for biological, chemical and physical mechanisms that are activated inside the reactor tank.

Moreover, it is important to show that some PhCs are not retained by the membrane system, for example those from more complex molecules or containing particular groups (Wen et al. (2004), Pauwels et al. (2006), Bouju et al. (2008)) because they remain in the dissolved phase and are not retained by the membrane.

Jacobsen et al. (1993) found that removal by sorption was important for pentachioropbenol (but the same is for PhCs) and was up to 50% of the total removal at short SRTs ($<$ 3 days), decreasing to 5-10% at higher SRTs ($>$ 14 days). There are two reasons to expect that sorption in bioreactors with low SRTs will play a more important role than for bioreactors with high SRTs: (i) at low SRT, the slow growing specific degraders will be washed out from the reactor system. Consequently, biodegradation is stopped and the concentration level in the bioreactor increases, which leads to an increased sorption and (ii) a higher mass-flow of wasted biomass will contribute to an increased removal of pollutants in the sorbed phase.

Many studies like Ternes et al. (2004a), Pauwels and Verstraete (2006) and Jones et al. (2005a) and the European project Poseidon (Ternes and Joss (2006)) made by many Europeans research groups agree on the necessity to pay more attention to the microbiological and chemical nature of the waste in question (the hospital).

Another important point is about the pollution load of this particular WWs, difficult to treat for the qualitative and quantitative characteristics, especially in view of the final point of discharge and mainly its intended use.

In conclusion for the most appropriate treatment for HWWs, there is a preferred sequence to recommend and in general:

- a separate treatment for HWWs is recommended in order to avoid dilution due to mixing with urban sewage during co-treatment
- a biological treatment is necessary to remove organic load. Longer SRT and high concentrations of the biomass in the biological tanks favour all the biodegradation processes. UF membrane technology seems to be a promising means for removal of pharmaceuticals; these treatments should be optimized by modification of the membranes (variation of the materials and reduction of molecular mass cut-off limits) and or by modification of the treatment process (inoculation of specific microorganisms)
- ozonation and AOPs are at present considered promising techniques due to the fact that they can react with many recalcitrant compounds, resulting in a more biodegradable effluent;
- GAC and PAC can enhance the removal of many PhCs.

Further studies and experimental investigations are required in order to evaluate the capacity for removing the main PhCs from WWs by the different treatment steps and to provide information about the most efficient ones from a technical and an economic point of view.

As already stated, there is no specific treatment able to remove, at high percentage, all kinds of micro-pollutants typically found in HWWs due to their differing behaviour during treatments. Many PhCs are resistant to conventional treatments. According to Pauwels and Verstraete (2006) different operational configurations should be developed and calibrated, thus generating the potential for practitioners to be informed about the financial aspects and overall risks associated with putative treatments of HWWs.

Tsakona et al. (2007) proposed that the waste management strategy applied at the hospital was observed and problematic areas were determined. All stages of waste management presented problems, which mainly were due to human neglect. To overcome these obstacles, the following actions were proposed for each stage of waste management. These concept are explained in figure 5.10 where a schematic representation of the waste categories and the proposed treatment and disposal methods at the hospital were presented.

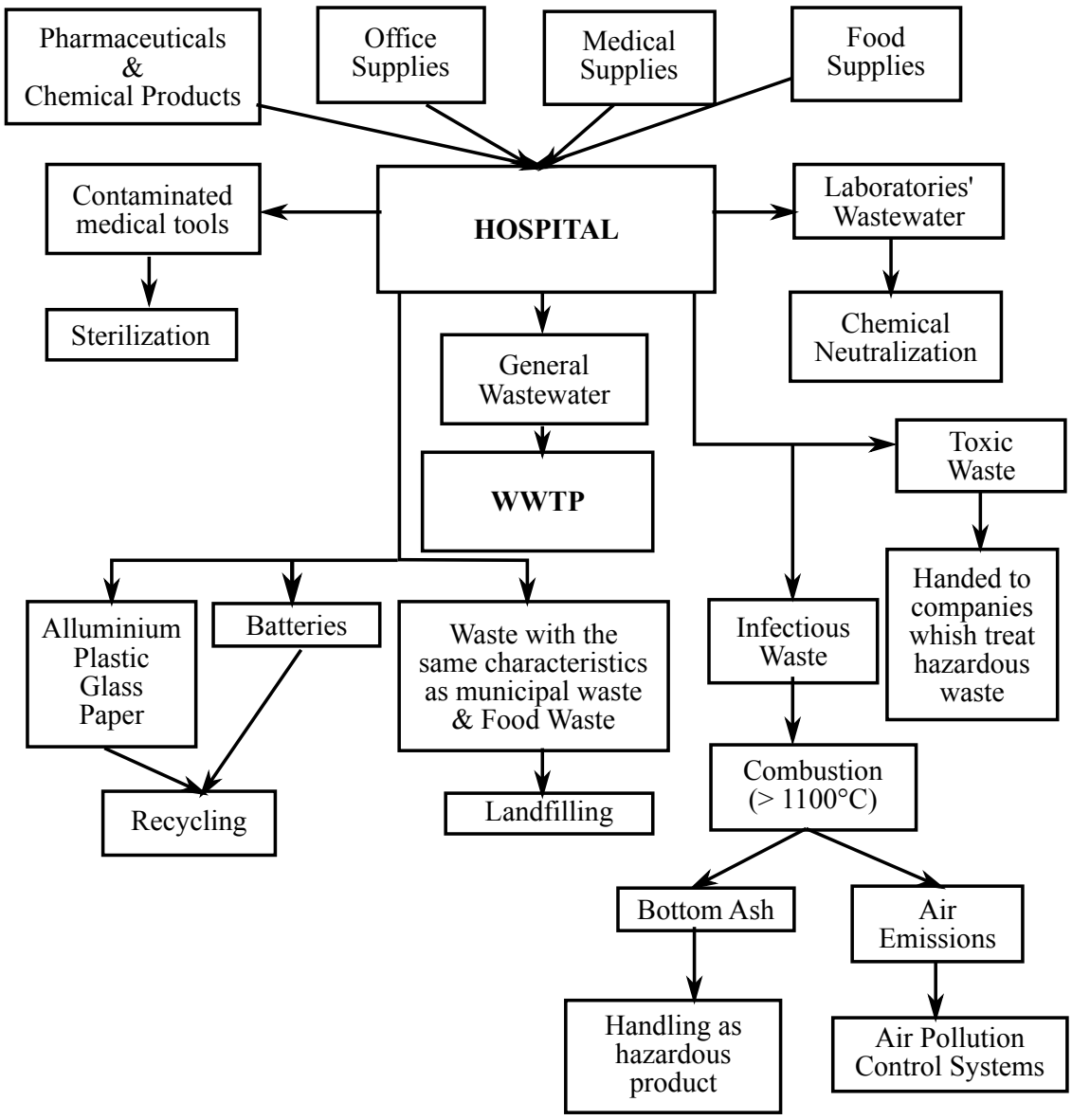


Figure 5.10.: Schematic representation of the waste categories and the proposed treatment and disposal methods at the hospital where research was conducted. From Tsakona et al. (2007)

Beier et al. (2011) report an experimental investigation about MBR on HWWs and they conclude that MBR are a very attractive option for the treatment of these kind of waters and elimination of PhCs in high density urban areas. The investigation showed that, depending on the substance, between 19% and 94% of the level of antibiotics found in the environment originate from hospitals. Because of their ecotoxic potential, HWWs can have a significant impact on the environment. The segregation of these WWs and their separate treatment at the source can reduce the entry of drugs in waterways and enable water reuse after adequate polishing treatment processes.

Beier et al. (2011) confirm the appropriateness of MBR for the treatment of HWWs in high density urban areas. Based on a mass balance in an appropriate large-scale case study, it was shown that the proportion of antibiotics found in UWWs originated to at least 34% from the hospital. Because the pharmaceuticals concentration in the MBR effluent is often higher than the target value of 100 ng L^{-1}, it is recommended to add an advanced treatment technology, such as activated carbon adsorption, ozone treatment or a further membrane step (nanofiltration or reverse osmosis) after the MBR process. This also creates new opportunities for water reuse. It should be mentioned that the residual streams emerging from the treatment of HWWs (such as sludges and screenings) require thermal disposal. In new hospital buildings, the streams containing pharmaceuticals should be segregated at the source and separately treated, for example in MBRs. This would avoid the discharge of these compounds in the sewer network and later on in the environment.

Interesting definitions about *Source control* and *waste design* are reported in Larsen and Gujer (2001) and resumed in figure 5.11.

Referring to hospital effluent management, many scientists agree in recommending the avoidance of co-treatment with UWWs and of dedicating separated treatments for HWWs (Pauwels and Verstraete (2006)). Heinzmann et al. (2008) suggested in evaluating the feasibility of collecting in a separated sewage the effluents from specific wards containing, for example, X-ray contrast media. Larsen et al. (2004) and Ternes et al. (2004a) found that source separation of urine (see also section 5.3), containing many of the pharmaceuticals and their transformation products from human metabolism, may offer the most effective solution to the problem of pharmaceuticals

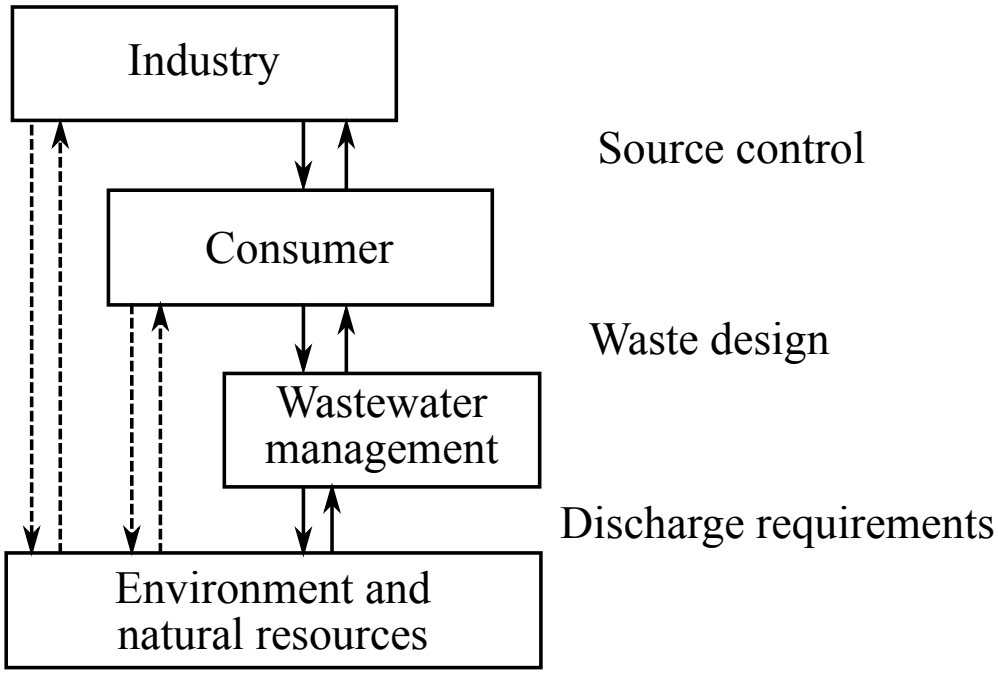


Figure 5.11.: Source control waste design and discharge requirements relate to different interfaces between the relevant systems. From Larsen and Gujer (2001)

in the environment. Due to the higher concentrations of micro-pollutants, biological as well as physical processes are expected to be more efficient for urine than diluted WWs. However, economic feasibility must be carefully evaluated.

Referring to the best available technologies in removing PhCs from WWs, recent studies, generally investigating UWWs or synthetic ones, show that there is not a unique treatment sequence able to remove all kinds of micro-pollutants, due to their differing behaviours. Their main removal mechanisms are biodegradation favored by a long sludge time (more than 30 d) and adsorption onto sludge flocks (Jones et al. (2005a); Castiglioni et al. (2006); Lindberg et al. (2006); Pauwels and Verstraete (2006); Matamoros et al. (2008); Miege et al. (2008)). Chemical-physical treatments like coagulation-flocculation precipitation are not efficacious (Ternes and Joss (2006)), while secondary biological treatments are considered to be an effective barrier for most PhCs due to the metabolic and co-metabolic processes (Kreuzinger et al. (2004); Daigger et al. (2005); Kimura et al. (2007); Radjenovic et al. (2009)) which can take place in these systems. As many micro-pollutants tend to adsorb/absorb into the biomass flocks, an efficient solid/liquid separation can greatly improve their removal from wastewater and, at the same time, guarantee a constant and really

good effluent quality. Membrane biological reactors (MBRs) are suggested by many authors (Daigger et al. (2005); Pauwels et al. (2006); Radjenovic et al. (2009)). Ozonation and advanced oxidation processes (AOPs) are promising for an efficient degradation of PhCs in water and wastewaters (Zwiener and Frimmel (2000); Chiang et al. (2003); Huber et al. (2003); Balcioglu and Otker (2003); Ternes et al. (2003); Machado et al. (2007); Zimmermann et al. (2008)).

Pauwels and Verstraete (2006) explain that HWWs urgently merit to be addressed as critical discharge to the environment in both developing and industrialized countries. In view of the above mentioned features, it is clear that HWWs is a complex matrix which warrants treatment before discharge to the environment.

About the HWWs, Boillot et al. (2008) conclude that hospital effluents are still rather poorly understood and in a context in which hazardous substances are accused, it appears necessary to carry out an in-depth characterization of this type of effluent. Hospitals are recognized for the specific substances they use: chemical reactants, disinfectants, detergents, drug residues, etc. In his studies Boillot et al. (2008) reports the global physicochemical parameters highlight moderate organic pollution of the effluents. However, a certain number of specific pollutants were measured at non-negligible concentrations: AOX, glutaraldehyde, free chlorine, detergents, Freon 113 and alcohols, acetone, formaldehyde, acetaldehyde, ammoniums, phenols as well as several metals (copper, lead, zinc and arsenic). Generally, there was very little bacterial flora in the effluents. In addition, a battery of detail bioassays showed a considerable level of ecotoxicity with contributions made to toxicity linked to TSS at certain periods. The study also showed that major fluctuations of pollution occurred during the day. These physicochemical, microbiological and ecotoxicological variations were correlated with hospital activities (change of shift, cleaning and care activities, cleaning operating theatre units, progressive ending of activities and night).

Liu et al. (2010) reports that of the 94 hospitals in Beijing, 89.6% use chlorine-containing disinfectant for sewage treatment, in which liquid chlorine disinfection accounted for 56.3% (figure 5.12); 84.6% of the 36 hospitals in Kunming use sodium hypochlorite disinfectant in 2004; and 63% use liquid chlorine and 35.8% use chlorine dioxide disinfection of the 106 hospitals in Hangzhou in 2004.

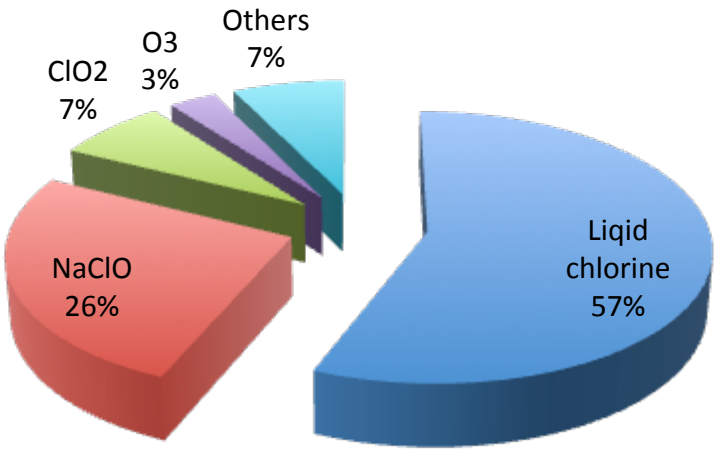


Figure 5.12.: Disinfection types of 94 hospitals in Beijing. From Liu et al. (2010)

5.5. Experimental investigation

An experimental investigation was carried out during 2007 and 2008 on the effluent of a 300 bed hospital in Lagosanto near Ferrara and on the influent to the Lagosanto municipal WWTP (5000 population equivalent, i.e.), in order to chemically characterize these two kinds of WWs, as reported in section 4.2. The hospital has a wide spectrum of wards (surgery, anaesthesiology and intensive care, orthopaedic and traumatology, obstetrics and gynaecology, paediatrics, gastroenterology, cardiology, urology, neurology, psychiatric) and services (first aid, radiology and diagnostic, dialysis, clinical analysis) and thus may be considered representative of a general hospital.

When a large hospital is built in the outskirts of a big town, it may be more convenient, from a technical and economic view point, to convey HWWs to the nearest existing WWTP or to build a new one for hospital effluent only. The existing WWTP could have a small capacity. In these cases, advanced treatments are recommended in order to protect and safeguard the environment, by reducing the pollutant load discharged with the final effluent. As reported, MBR technology seems to be, at present, the most adequate one. For this reason, an MBR pilot plant (whose main characteristics are reported in table 4.8) directly fed by Lagosanto Hospital effluent was tested. The chemical characteristics of the permeate are reported in Table 5.1.

Table 5.1.: Samples number and chemical characteristics of the permeate during the observation period

Parameter	**Samples**	**Average**
BOD_5, mg L^{-1}	20	9.2 ± 6
COD, mg L^{-1}	20	20 ± 10
$COD_{filtered}$, mg L^{-1}	20	15 ± 8
SS, mg L^{-1}	20	2 ± 1
N-NH_4, mg L^{-1}	20	2 ± 1
Total P, mg L^{-1}	20	4 ± 1
E. coli, CFU/100 mL	20	< 10

Very low concentrations were measured for all the monitored parameters, in particular for SS and *E. coli*. These good results are due to the combined actions of biological degradation in the reactor and excellent solid-liquid separation due to UF membrane filtration. In fact, MBR operates at a higher biomass content (10-12 kg m^3) and with longer sludge retention times (SRT) of up to 30-50 days. In this way, a more diverse microbial community can be established, including slow growing specialized bacteria with broader physiological capabilities; metabolic and co-metabolic processes can be intensified which will also affect recalcitrant compounds and a more complete mineralization can be possible in accordance with Clara et al. (2005a); Daigger et al. (2005). These processes are the most important and efficient biological systems for removing PhCs. Moreover, due to the small pore size (0.01 μm) of the UF membranes used, we expect that they are also able to retain the viruses typically present in HWWs, reported below, whose dimensions vary in the range of 0.02-0.16 μm.

HWWs characterization. Monitored parameters for HWWs have been: BOD_5, COD, SS, N-NH_4, Total N, total P and *E. coli*. Instantaneous water samples were withdrawn monthly from the internal hospital sewage network before immission into public sewage. The hospital sewage network receives and conveys only black waters from the different wards and services, as rain waters have a separate collection system. Water samples were collected in new 1 L plastic or glass bottles and immediately analyzed for the different parameters.

UWWs characterization. During the observation period, instantaneous samples of water from the influent of the municipal WWTP of Lagosanto (5000 i.e.) were withdrawn monthly and analyzed using the same parameters as HWWs. In addition, historical data sets were used for its characterization. Samples were never taken while it was raining, but about 24 h after the rain had stopped. This practice was followed in order to avoid dilution of pollutant concentrations in wastewaters due to the fact that this WWTP receives combined sewage (municipal wastewaters as well as rain water).

The studied pilot plant. A submerged MBR pilot plant of 1.5 m^3 active volume equipped with ultrafiltration (UF) shallow fiber membranes, purchased from Puron, was installed at the Delta Hospital and fed by its effluent. In this section is considered also the UF technology because with a view to the new project of Cona Hospital this seems the best technology to adopt.

The main characteristics of the studied pilot plant are reported in table 4.6 and also in section 4.2. In particular this section refers to the UF MBR reported. The biocenosis of the MBR was grown from inoculated sludge from the Lagosanto municipal WWTP (aeration basin) and cultivated over a period of approximately 45 days to reach steady-state conditions. Continuous aeration was provided by means of a sparger pipe situated at the bottom of the reaction vessel; the oxygen concentration was kept between 1 and 2 mg L^{-1}. The temperature inside the reactor was 23 $\pm$ 4 ^oC throughout sampling.

Twenty WWs samples were taken bearing in mind the HRT of the MBR process for the influent to the pilot plant (corresponding to the raw hospital effluent) and the effluent (permeate).

Analytical methodology. Analyses of chemical parameters were performed according to the American Standard Methods for the Examination of water and wastewater. Counting of *E. coli* was performed by the membrane filtration method, as described in (IRSA-CNR (1994)), using the selective agar ECX GLUC AGAR at an incubation temperature of 44.5 $\pm$ 0.2 ^oC for 18-24 hours. For other information about the analytical methodology see appendix A.

5.6. Adopted WWs treatment sequence in new Ferrara Hospital

The new hospital complex in Ferrara is situated six kilometres from the town in the first outskirts, in the small urban centre of Cona. It has a capacity of 900 beds and a staff of 2400, including medical, administrative and technical services, in addition to 250 university students and elderly people staying in the on-site accommodations. Due to the building growth connected with the hospital construction, the nearby urban centres (Cona and Gualdo) are under expansion and their estimated residential population is expected to climb to 1700 persons over the next years. In addition, there are local businesses and industries, corresponding to 500 i.e.

Currently in this area, combined urban and industrial wastewaters (IWWs) are conveyed to a small WWTP at Gualdo designed for 1000 i.e. Treatment includes degritting, primary sedimentation, conventional activated sludge treatment and disinfection. This WWTP is not adequate to treat all the WWs coming from the new hospital and the new urban development. A feasibility study has been carried out to compare different scenarios with the aim of highlighting the advantages and disadvantages of each design solution (figure 5.13).

a. Treat the HWWs on site by adopting the best available technology, and reuse them for irrigation purposes (mainly for hospital parkland), convey UWWs and IWWs to the small WWTP at Gualdo, upgrade it to the whole predicted flow rate and treat together the two kinds of effluents. Treat all the sludge (including that from HWws treatments) at the WWTP at Gualdo (Figure 5.13 (a)).

b. Convey the HWWs by pipeline to the main WWTP in Ferrara, about 10-15 km away from the new hospital, convey UWWs and IWWs to the small WWTP at Gualdo, upgrade it to the whole predicted flow rate and treat together the two kinds of effluents (Figure 5.13 (b)).

c. Convey all the three WWs to the small WWTP of Gualdo, upgrade it for IWWs and UWWs treatment and build a dedicated line for advanced treatment of HWWs (Figure 5.13 (c)).

d. Convey to and co-treat all three kinds of wastewaters at a new WWTP which, once completed, will make the current WWTP of Gualdo obsolete (Figure 5.13 (d)).

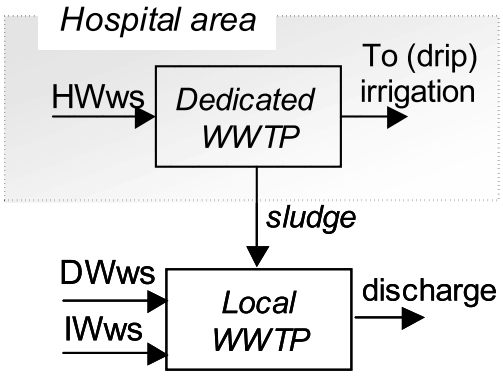
The final effluents of each scenario is in any case, in compliance with the (Italian) legal limits for all conventional pollutants (BOD_5, COD, SS, nitrogen compounds, phosphorus compounds, *E. coli*, ...) corresponding to its final destination: discharge into surface water body (D. Lgs 152/2006) or direct reuse for irrigation (DM 185/2003) (table 5.2). The choice of the most adequate scenario to adopt depends on many technical, economical, legal, environmental, social, as well as political constraints. Figure 5.13 focuses on the main technical aspects concerning the management and the treatment of a large hospital complex effluent in a small urban centre. In particular the different scenarios for HWWs management and treatments. Flow rates for this case study: HWWs = 630 m^3 d^{-1}; UWWs = 300-500 m^3 d^{-1} the range is due to future urban development; IWWs = 50-70 m^3 d^{-1}; Ferrara UWWs = 20 000 m^3 d^{-1}

Table 5.2.: Main Italian legal requirements for effluent discharge into surface water body and for reuse

Parameter	**D. Lgs 152/2006 Discharge**	**D.M. 185/2003 Direct Reuse**
COD, mg L^{-1}	125	100
TSS, mg L^{-1}	35	10
BOD_5, mg L^{-1}	25	20
N-NH_4, mg L^{-1}	15	2
Total P, mg L^{-1}	10	2
E. coli, CFU/100 mL	$5{\cdot}10^3$	10 as 80th percentile; 100 as the maximum value

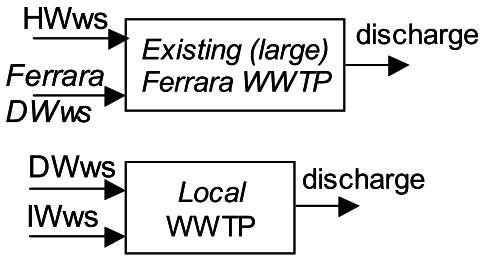
The last option was selected for the treatment of hospital, urban and industrial WWs in the study site for the following reasons:

- hospital flow rate will represent the greater part of the whole WWs flow rate to be treated for the next 5-10 years, as the nearby urban centres will take longer to be completed
- existing overflows along the network for urban and industrial sewage regulate the flow inside the pipes and guarantee a maximum flow rate at the WWTP



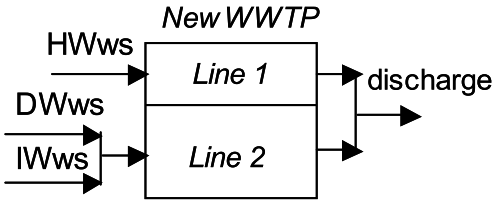
(a)

Advantages: Different sequences of treatment depending on the WWs, more appropriate treatments for HWWs; possibility of reusing the final effluent of the dedicated WWTP for drip irrigating the hospital green area. Drawbacks: Two WWTPs in operation



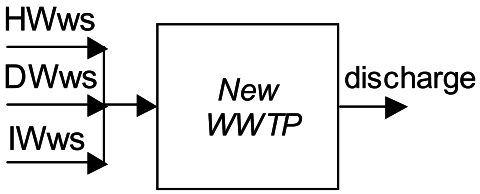
(b)

Advantages: Greater dilution of HWws. Drawbacks: Storm water overflows hamper biological processes at the (large) WWTP



(c)

Advantages: Just one WWTP, more appropriate treatments for HWWs, just one discharge point. Drawbacks: Higher operational costs



(d)

Advantages: just one discharge point. Drawbacks: Advanced treatments may not be necessary for UWWs Combined sewage must be previously drained in case of MBR

Figure 5.13.: Different scenarios for HWWs management and treatments

- the sewage systems of the urban centres under expansion are separated and only black WWs will be conveyed to the WWTP. White WWs will be treated separately.

The adopted sequence of treatments is reported in figure 5.14. Design parameters of the biological section result from the experimental investigation on the hospital effluent and on the MBR pilot plant previously described; those referring to ozonation/UV irradiation derive from literature specific data (Ternes and Joss (2006)). The average wastewater flow rate is about 60 m^3 h^{-1}. Hospital effluent and urban-industrial WWs are pumped separately, then subjected to a degritting and a biological treatment (dephosphoration - nitrification - denitrification) by an MBR (SRT = 30 d; biomass concentration of 8-10 kg m^{-3}, UF membranes with pores size of 0.05 μm, a surface flux of 15-25 L m^{-2} h^{-1}). The permeate is subjected to an AOP by means of O_3 (7.5-10 mg O_3 L^{-1}, contact time of 16 min) and UV (irradiation of 100 mJ cm^{-2}, exposure time of about 4-7 s).

Figure 5.14 Flow scheme of the new WWTP for HWWs, UWWs and IWWs.

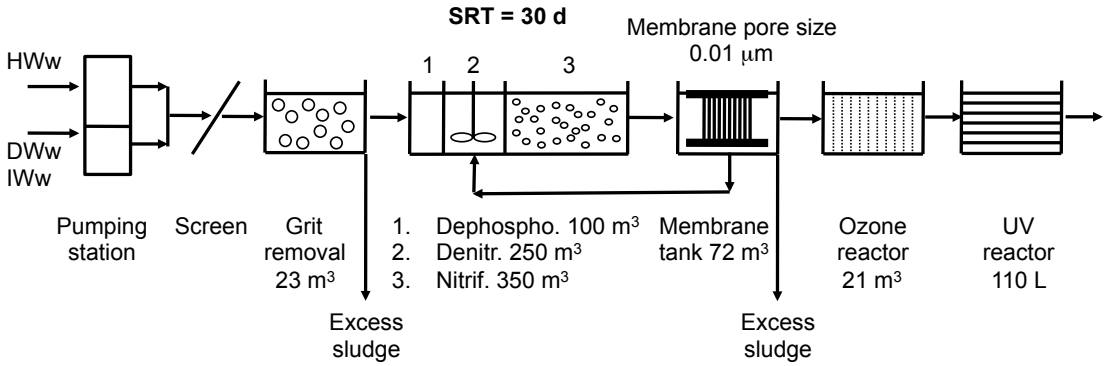


Figure 5.14.: Flow scheme of the new WWTP for HWWs, UWWs and IWWs

For the sludge, technologies able to greatly reduce its production and disposal frequency have been adopted: first, an aerobic digestion; second, an ozonation (50 g O_3 kg^{-1} TSS^{-1} treated) of the digested sludge, which reduces the excess sludge amount and favours oxidation of the PhCs absorbed into the solid phase, increasing the content of readily biodegradable COD, and third, a mechanical thickener completes the treatment.

Average influent concentrations were obtained by assuming that HWWs contribute 60% of the total influent flow rate and UWWs the remaining 40%, and by weighting

their corresponding (average) values from the second column in table 4.6. Concentrations in the MBR permeate are prudently taken as equal to those reported in Table 5.1, resulting from our experimental investigation, with the exception that total P as a specific chemical treatment is included (Table 5.3). The final effluent, after AOP treatment, will have a better quality in terms of macro-pollutants as well as of PhCs (antibiotics, analgesics and anti - inflammatories) due to the combined action of ozone and UV on recalcitrant compounds and less biodegradable organic matter still present in the water. According to literature data (Bouju et al. (2008); Kasprzyk-Hordern et al. (2009); Radjenovic et al. (2009)), their removal range is from 50-90%. At present, these seem to be the best available technologies for removing different kinds of micro - pollutants.

This produces an effluent of really high and constant quality, which is also able to meet the strict Italian limits for discharge into surface water bodies and with an adequate dose of ozone and radiation, legal limits for direct reuse will also be satisfied. Its receiving surface water body is a narrow canal with a modest autodepurative capacity belonging to the local network, usually used for agricultural needs. The ability to guarantee a WWTP effluent of excellent quality reduces its impact on the environment.

These reasons supported the adoption of biological and chemical advanced technologies for the treatment of hospital, urban and industrial WWs. Moreover due to the small size (60 m^3 d^{-1}), this new WWTP could be used as a *test* plant for further experimental investigations in order to optimize removal of micro-pollutants and evaluate the economic-technical feasibility of these kinds of technologies in other sites.

Table 5.3.: Main design parameters and final permeate quality

Parameter	**Influent**	**Effluent**
COD, mg L^{-1}	355	20
SS, mg L^{-1}	137	2
BOD_5, mg L^{-1}	164	9
N-NH_4, mg L^{-1}	25	2
Total P, mg L^{-1}	5	1
E. coli, CFU/100 mL	$5{\cdot}10^5$	5

5.6.1. Footprint and costs

Joss et al. (2008) explain that activated sludge treatment allows only for a partial removal of micropollutants, mainly via sorption and biological degradation. Ozonation and activated carbon filtration are processes bearing the potential to drastically reduce the micropollutant load discharged to the environment after (centralized) biological treatment. The estimated total costs between 0.05 and 0.20 Euro m^3 treated water (depending on plant size and effluent DOC content) represent only a small fraction of the total costs for UWWs management and are therefore considered feasible.

Ternes et al. (2003) report that, for large-scale installation (investment + 10 g m^3 ozone) the costs for the ozone treatment, are approximately < 0.04 Euro m^3 and for ozone/UV (400 J m^{-2}) < 0.05 Euro m^3.

The new WWTP for the new Ferrara's Hospital covers an area of 1 000 m^2, resulting in a specific area of 0.25 m^2 $i.e.^{-1}$.

Specific construction costs amount to 460 Euro $i.e.^{-1}$ and 3.6 Euro m^{-3} for treated WW.

In total the energy consumption amounts to 830 MWh yr^{-1}, this cause an annual cost of 100 000 Euro.

The final treatment of the excess sludge production (100 tn yr^{-1}) will be with ozone and this will involve in a gross economic output of 59-88 Euro ton^{-1} of sludge not disposed.

5.7. Discussion

Informed scientists agree that urgent measures must be taken in order to set guidelines for the treatment of HWWs, both with respect to attainable efficiency and costs per m^3 of water treated. Experimental studies are also necessary, because there is a remarkable paucity of data, concerning the possible impacts of HWWs on the environment.

The case study presented and discussed here shows how the delicate problem of the treatment of the effluent of a new large hospital built in a small urban centre has been faced. Different operational configurations were evaluated and compared,

thus generating the potential for administrators and practitioners to be informed on financial aspects and technical solutions for the different treatment options of HWWs. The sequence adopted for the treatment of the effluent of the new large hospital in Ferrara results from an experimental investigation. It represents, up to now, the best available technology for removing macro - pollutants as well as PhCs, as it combines advanced biological and chemical treatments, resulting in a reduced impact of the final effluent on the environment.

Moreover also the footprint and the costs are considered and the final treatment sequence was chose on the basis of literature data and experimental investigation in order to reduce the final impact of this new hospital into the environment.

The adopted treatment (reported in the scheme in figure 5.14) represents the best balance between cost and possibility to built this new treatment plant. Obviously a dedicate WWTP treating only HWWs were done the best treatment for this particular kind of WWs, but the demand to treat also the local UWWs in the same WWTP require to built only one treatment plant with the best technologies.

Ort et al. (2010) show that if, for whatever motivation, HWWs shall be treated separately onsite, it must be noted, that for many substances no major overall reduction can be achieved, since many PhCs are taken on a regular basis at home. With the current trend to shorter hospitalisations and treatments (diagnostics) of outpatients, this also holds true for compounds mainly administered in hospitals.

Beier et al. (2011) explain that German Ministry of the Environment set a limit of 100 ng L^{-1} for the discharge of PhCs into the environment and the measured eliminations correspond to a large extend values cited in the litterature for membrane bioreactors (see Ternes (1998), Joss et al. (2006)). The sludge age in the MBR treating HWWs exceeded 100 days. The elimination of PhCs in the MBR is based on adsorption of the compounds on the activated sludge matrix and on biological degradation or transformation.

Considering that for many pharmaceutical compounds, the concentration in the MBR effluent is often higher than the target value of 100 ng L^{-1}, it is recommended to add an advanced treatment technology, such as activated carbon adsorption, ozone treatment or a further membrane step (nanofiltration or reverse osmosis) after the MBR process.

Joss et al. (2008) conclude speaking about the advanced treatment of wastewater that is probably one of the simplest measures on a short term. On a longer term, more efficient source control measures for impeding environmental contamination with micropollutant may be implemented.

CHAPTER 6

Conclusions

The aim of this work was the definition and the characterization of HWWs with particular attention to the possible differences between these effluents and the urban ones.

The presence of a hospital structure in an urban area represents a source of impact for many pollutants (mainly the common monitored macroparameter) and for *new* emerging contaminants (antibiotics, hormones, surfactants, detergents, fragrances, heavy metals...).

Emerging contaminants are represented by different categories of drugs and, among them, antibiotics are the main common into the HWWs as reported in this study and confirmed by the literature data.

The starting point of this research was the critical analysis of the current management of hospital effluents, generally immitted into the public sewage and the co-treatment to a municipal WWTP. In this context, quali - quantitative analysis of hospital and urban raw effluents were carried out and evaluation of the efficiency of conventional and advanced technologies were done in order to focus and understand the best treatment for hospital effluents which minimizes the environmental impact.

This work started in chapter 2 from the analysis of 73 emerging contaminants from surface, ground waters and drinking waters deriving from Po River and Ferrara

waters work. These analysis were done in order to obtain some informations about the diffusion into the environment of these particular pollutants. A comparison with literature data were done.

An important consideration is about the concept that all the discussion and the mass balance done during this thesis referring to the analysed compounds (73 in Ferrara for example) and not to all the possible compounds present in the waters or discharged. This concept is to take in consideration because perhaps some compounds not analysed in this study could change some balance mainly in surface waters. So, all the consideration here reported refers to the big number of analysed compounds, but not to all the possible compounds.

Table 2.5 compares the analytical results reporting that the drinking water processes improve the water quality also towards PhCs. Referring to the GW analysis (table C.3) it is clear that all the high concentration of these PhCs is due only to 4 different compounds: Indomethacine, Ketoprofen, Mevastatin and Doxycycline. If summed, they represent more than 70% of the total concentration. In general, the accumulation of the PhCs in GWs is possible but, the aerobic, anoxic or anaerobic conditions in this particular sites can differ a lot and can vary from point to point influencing the stability and the accumulation of these substances.

The detected compounds decrease from the GWs (36 compounds) to the Po River waters (27 compounds) till the wells waters (10 compound detected).

Next chapter (chapter 3) analyses the hospital effluent, studying the macrocharacteristics of these waters. This chapter take in consideration the common management of hospital effluent, with a general point of view and conclude with some important aspects about hospital structures:

- **Pollutant load**. Referring to this topic table 3.4 shows the ratio about macroparameters in the two effluents, and table 3.8 shows the ratio in the different classes of micropollutant compounds. It is evident that the hospital pollutants load is really higher than those in UWWs. The ratio can be also 3 times higher for the common BOD_5, COD, SS and 4, 10, till 150 for the reported micropollutant. For example hospital structures represent, potentially, a consistent antibiotic input sources into the sewage and consequently into the environment, for the main use of antibiotics in these structures, so they

can do a really important contribution to the proliferation of drug-resistant microorganisms.

- **Hydraulic contribution**. Figures 3.3 and 3.4 show the water consumption per day and per bed with respect to hospital size, and the flow rates for hospital and urban centres of different size. Daily HWWs flow rates range between 600-900 L bed^{-1} d^{-1} and so they are 2-5 times higher than urban flow rates, which refer to one inhabitant equivalent (typically included in the interval 120-250 L $i.e.^{-1}$ d^{-1}).

Moreover this chapter reports the analysis done in the effluent of the two studied hospital, Ferrara and Lagosanto. About these hospital some important consideration are:

- HWWs are subject to seasonal variations (see table 3.15) and, in fact, the experimental campaign results from summer and winter are considered separately in table 3.16.

- In terms of detected compounds, Lagosanto shows a higher value, if compared both with Ferrara summer analysis than with Ferrara winter analysis. In particular, in Lagosanto WWs were found 59 compounds. In Ferrara WWs there were a large variability from summer (47 compounds) to winter (57 compounds).

- The more detected compounds are the two antibiotics Ciprofloxacin and Ofloxacin and the diuretic Furosemide. Moreover in Ferrara Hospital was detected also a hight concentration of the antibiotic Clarithromycin. These compounds were detected in a low concentration in Lagosanto Hospital than in Ferrara Hospital.

- Table 3.16 shows the pro capita contribute of the PhCs. The small hospital of Lagosanto presents a really highest pro capita load (expressed as ng L^{-1} $patient^{-1}$) if compared with that of Ferrara. The 5.8 ng L^{-1} $patient^{-1}$ are really a high contribute compared with the Ferrara summer values of 0.8 ng L^{-1} $patient^{-1}$. In total, referring to the reported analytical results, the sum of PhCs for patient are 305 ng L^{-1} $patient^{-1}$ in Lagosanto Hospital and *only*

38 (or 127) in Ferrara Hospital in summer (or in winter season). This is also due to the lowest water consumption in Lagosanto Hospital (670 L bed^{-1} d^{-1}) respect Ferrara Hospital (800 L bed^{-1} d^{-1}).

- This problem put the attention on the characteristics of the WWs derived from a small hospital structure (Lagosanto for example) that, in terms of pollutant load, may represent an environmental problem, if does not adequately treated before the discharge in a surface water body.

  Lagosanto's WWs are collected in a public sewage and co-treated with UWWs in a CAS system (5000 i.e.). The final discharge point is an irrigational channel with a dominant flow derived from the WWTP for almost 8 month for year. Ferrara WWs are also collected in a public sewage but co-treated with the UWWs derived from all the town (130 000 i.e.) and mixed, before the discharge in the final water body, with the industrial treated WWs derived from the nearest petrochemical site (100 000 i.e.). Then, in this case, the dilution with other kind of waters, plays a really important role in the final concentration before the discharge. So the impact of this WWTP on the final discharge is really low in terms of PhCs concentration.

A lot of experimental investigation were carried out during this research years and almost 6 different pilot plants were tested in order to investigate and focus the problem under studying. To see all the experimental investigations and the pilot plants tested, a rapid focus is presented in appendix B.

The analysis done about the *simple* disinfection of raw hospital effluents shown that:

- PAA is able to reach higher removal rate for TC than *E. coli* (0.5-1 log unit of difference on average at the same applied dose c x t) (Figure 4.3).

- On the contrary, NaClO is a bit more effective with *E. coli* than TC (Figure 4.4).

- Experimental data are quite spread due to the different characteristics of the raw WW, influent to the pilot plant, in particular suspended solids that varied in a wide range (table 4.4). About this table some considerations are according

to literature data, a concentration of SS up to 100 mg L^{-1} does not influence the biocidal action of PAA. Greater concentrations can reduce it.

The disinfection of raw HWWs with PAA or NaClO represents a good technical solution for those situation, where is not present a WWTP able to treat this specific WWs and in order to reduce the health risk the disinfection is recommended.

The experimental section about the two tested MBRs in Lagosanto (section 4.2) reported the results about the typical pollutant substances (macroparameters) and not about PhCs. The results of these experimental sections confirm that an UF membrane is able to reduce the final impact of the hospital effluents due to the excellent water quality obtained.

Other studies (from section 4.3 to section 4.6) focus the attention of CAS, MBR, O_3 and CW technologies in removing PhCs in order to see the capacity of conventional, advanced biological and oxidation processes and a natural polishing system in removing the investigated micropollutants.

The main results confirmed that a multibarrier system (obtained in different ways: an MBR + O_3 and a CAS + CW) can improve the water quality by guaranteeing a higher removal efficiency mainly for those pollutants that are present in low concentration in WWs.

A typical CAS treatment (SRT = 5 d) is able to remove the carbonaceous fraction (COD, BOD_5) and the nutrients (N and P) present in WWs but not all the pollutants detectable in concentration with from μg L^{-1} to ng L^{-1}. This because the typical biological treatment needs time and quantity to develop bacterial and biomasses, able to degrade and transform also the micro-compounds.

The results about the natural treatments put in evidence that the persistent mass loading due to PhCs of a secondary effluent can be reduced by a polishing treatment, able to favour different removal pathways, which become necessary due to the great variability of the contaminants of interest.

CW requires high surface i.e.$^{-1}$ ratio, so these natural polishing treatments represent adequate solution for small communities or the last treatment step for the dedicated treatment of specific users, such as hospital structures where the concentrations of micropollutants should be more carefully removed. The natural treatment can improve the final efficiency because the coexistence of several microenvironments

in CWs allows both the thermodynamic feasibility of chemical reactions and the development of a great variety of microbiological communities able to guarantee the enzymatic capacity necessary to achieve the target biogeochemical reactions. This is true for the low concentrations of PhCs detected in the first experimental investigation (section 4.5) but also for the second one (section 4.6) where the concentration of three antibiotics were artificially increased in order to simulate a peak concentration and to stress the natural system.

The *problem* of the adequate treatment for the hospital effluents must be taken in consideration from the scientific community in order to set guidelines and to verify if the final water body receptor is able to receive the pollution load deriving from WWTP. In fact, if the receiving river is an effluent dominant (the hight percentage of water derived from WWTP), it becomes necessary to improve the quality of the discharge, in order to reduce the long term environmental impact.

The case studies presented and discussed in this thesis show how the delicate problem of the effluent's treatments of a new large hospital built in a small urban centre, has been faced. Different operational configurations were evaluated and compared, thus generating the potential for administrators and practitioners, to be informed on financial aspects and technical solutions for the different treatment options of HWWs. The possible adopted sequences are shown in figure 5.13.

Recently many Authors (among them Ort et al. (2010) and Beier et al. (2011)) explain that it is recommended to add an advanced treatment technology, such as activated carbon adsorption, ozone treatment or a further membrane step (nanofiltration or reverse osmosis) after the MBR process, confirming that, in order to reduce the high load pollution derived from hospital structure, it is necessary a sequence of different consequent treatments. In these cases the adopted technology (such as nanofiltration or RO) represents the BAT but not the BATNEC. To obtain relevant results in removing PhCs from WWs, literature shows that it is possible to:

- make a reduction at the source of antibiotics. In substances the concept is to adopt other antibiotics, if possible, more degradable,
- make a source separation of the liquid part of the effluents with the solid phase. In fact, as reported, more PhCs tend to stay in urine rather than in faces. So an adequate liquid treatment can reduce the final environmental impact.

These two concepts represents some possible management ways that in some cases are quite expensive and difficult to respect and to implement.

The adopted treatment (reported in figure 5.14) represents, up to now, the best available technology in removing macro - pollutants as well as PhCs, as it combines advanced biological and chemical treatments, resulting in a reduced impact of the final effluent on the environment.

It is important to underline that today the dilution of HWWs plays an important role in the treatment. For example, a co-treatment of a large hospital in a densely populated catchment are causes a dilution in the total (urban + hospital) influent raw flow rate and consequently also in the final effluent, but it is appropriate to pay attention on the discharged load resulting from the contribute of the hospital and the urban center.

Table 3.17 put in evidence that the contact between UWWs and HWWs in Ferrara sewage generates a dilution of the concentration: from 1443 ng L^{-1} in Ferrara raw Hospital to 378 ng L^{-1} at the influent of Ferrara's WWTP.

Considering the 900 beds in Ferrara Hospital and the pro capite water consumption for bed in Ferrara (more or less 800 L bed^{-1} d^{-1}), it is easy to obtain the total flow per day in the hospital (720 m^3 d^{-1}). This value represents only the 2% of the total water conveyed at the Ferrara WWTP (more or less 35 000 m^3 d^{-1}).

Starting from the analytical results obtained in this thesis, considering the dilution factor ($\frac{Q_{Hospital}}{Q_{Total}}$) and comparing the hospital load with the urban ones, the percentage concentration of the hospital in the urban sewage represents 9% of the total load. This means that the hospital water load represents the 2% of the total water influent at Ferrara's WWTP, but the concentration load represent the 9% of the total PhCs in the municipal sewage. This is another important reason to consider hospital effluent quite different from the urban ones. The load percentage for the different classes are reported in table 3.17.

Another treated aspect confirms that a multibarrier system can really improve the final effluent quality in terms of quantity of detected pollutant and also in terms of load. In fact, a passage through a natural system working as polishing step, is able to reduce the concentration and the quantity of detected PhCs.

In a correct management of hospital structures, it is appropriate to consider their

effluent with all the problems that they can cause:

- hydraulic problems, due to their high water consumption. This represent an important *key design* to understand the future impact of an hospital structure into the sewage network,

- loading problems of the high concentration in macro and micro pollutants. This aspect represents a relevant problem mainly in small and old WWTPs that discharge in effluent dominant surface water body of the local surface network often used for irrigation purposes as it can occur in many countries,

- treatments problems for the difficult in defining the best sequence treatment due to the variety of behavior of the molecules of pharmaceuticals. Literature explains, and this study confirms, that the use of only one technology to treat this effluent is inadequate. CAS treatment treating only hospital effluents could be insufficient if the objective is the removing of high percentage of micropollutants. MBR represents a good technology, able to remove some micropollutants, but a multibarrier system is desirable. Advanced treatment, such as ozonation or natural polishing steps, are the best technologies that can activates chemical reactions and a great variety of microbiological communities, able to guarantee different biogeochemical reactions,

- discharge problems connected to the residual content of pharmaceuticals in the final treated WWs which can exhibits ecotoxicological effects. A correct evaluation of the final water receptor's characteristics (flow rate, dilution capacity, chemical characteristics, final destination, legal constrains) is really an important step in the planning of the building of a new hospital structure. The discharge problem is not a secondary question, because if the final discharge is in a large river, the resulting dilution and the natural processes (photodegradation) which can occur can contribute in the (natural) decrement of the pollutant concentrations and mitigate the consequent environmental impact, but, if the final effluent is a small channel, a continuous (bio-)accumulation of the pollutants can cause relevant environmental problems.

6.1. Suggestions for future work

In the last years the international literature developed numerous scientific publications about the PPCPs, PhCs, EDCs and micropollutants in general. There is no doubt that the *problem* of hospital effluents is relevant and the scientific community, mainly in the last years, is studying this aspect.

The definition of some markers for HWWs could be of great interest. For example in the UWWs treatment with three or four parameter (COD, SS, N...) it is possible to characterize the kind of effluent, but in the HWWs the high concentration of PhCs and the difference in the behaviour of these substances cause problem in the individuation of marker.

In general, scientists put the attention on Carbamazepine, Diclofenac, Sulfamethoxazole and Iopromide as markers of PhCs pollution in WWs. Referring to Carbamazepine it is considered as an anthropological marker and not a typical hospital substance, because it is commonly prescribed to outside patients for long periods and for many pathologies. Probably antibiotics could be markers for HWWs, but further studies are necessaries to define which kind.

An idea to characterize hospital effluents may be an analysis of toxicity of these WWs compared with the urban ones.

Another idea may be the study of an index of different parameter (macro and micro) in order to compare by the use of an aggregate function the different load of hospital and urban effluents.

APPENDIX A

Analytical methods

This Ph.D thesis does not deal with the analytical chemistry and this part of my thesis derives directly from my experience in the Barcelona CSIC Laboratory. I think that an analytical chemist, that will read this chapter could consider this part really a basic report, but the aim of this thesis was evaluate the PPCPs problem from an engineering point of view, so the analytical aspects (certainly important) are not the real core of this dissertation.

Analysis of conventional WWs parameters including COD, SS, NH_4 and total phosphorus, were performed according to the American Standard Methods for the Examination of water and wastewater APHA (2001). Counting of *E. coli* was performed by the membrane filtration method, as described in Ref. IRSA-CNR (1994).

Analysis on PhCs were conducted using the specific analytical method performed in Gros et al. (2009) described below.

For the pharmaceuticals analysis, water and WWs samples were collected in different forms by using clean plastic bottle in adequate volume:

- samples deriving from surface waters, ground waters and potable waters were collected in instantaneous samples
- samples taken from HWWs were collected directly from the final septic tank with an autosamples in order to have a 24 hours composite sample for each

point

- samples from Ferrara WWTP and from the CW studied before this plant. Each one of this samples was 4 hours composite sample

A.1. PhCs in environmental samples

The prerequisite for a proper risk assessment and monitoring of the quality of surface, drinking and waste water is the availability of multi-residue methods, that permit measurement at low ng L^{-1} level or even below that. A single method for the analysis of various pharmaceuticals belonging to different compound classes has several advantages, such as shorter analysis time, reduced field sampling and overall cost reduction. In the need to monitor pharmaceutical residues in the environment numerous sensitive, accurate and reliable analytical methods have been developed for determination of pharmaceuticals and their metabolites in aqueous solutions. The pharmaceuticals more frequently included in such multi-residue methods are analgesics and anti-inflammatory drugs, antibiotics, lipid regulators, psychiatric drugs, and β-blockers. These drugs have very high consumption worldwide and are the most ubiquitous in both surface and WWs. Solid-phase extraction (SPE) methods combined with gas chromatography-mass spectrometry (GC-MS) and GC with tandem MS (GC-MS2) (Halling-Sorensen et al. (1998)) or liquid chromatography (LC) with tandem MS (LC-MS2) (Stolker et al. (2004), Gros et al. (2006)) are the usual methods of choice for identification and quantitation. Furthermore, in the last few years, analytical methodologies using high performance LC (HPLC) or ultra performance LC (UPLC) coupled to advanced chromatographic techniques and detection systems such as quadrupole-time of flight (QqToF), ion trap (IT), quadrupole-linear ion trap (Q-LIT), linear ion trap-Fourier transform-ion cyclotron resonance (LIT-FT-ICR) and LTQ Orbitrap have been developed (Radjenovic (2009)).

Optimisation of the sample preparation step is one of the most important step in the development of an analytical method, since it will greatly influence the sensitivity and selectivity of the method. Target compounds are isolated and preconcentrated from the aqueous phase in the SPE enrichment step. Newly developed polymeric sorbents with improved wetting characteristics and mass transfer, and with additional

possibilities for interaction of functional groups of analytes have allowed high preconcentration factors. One of the major advantages is the possibility of carrying out a multi-residue method working at neutral pH (Gomez et al. (2006)), which greatly simplifies the sample handling procedure. Due to the high retention capabilities of these sorbents, acidic compounds can be extracted from water samples without previous acidification. This is of great importance when performing a multi-residue analysis, because the risk of acidic hydrolysis of other compounds is not enhanced. Furthermore, no clean-up step is needed for the removal of humic and fluvic acid, and also there is a possibility of online extraction using large sample volumes (Farre et al. (2007)). SPE and solid-phase microextraction (SPME) are the two most widely used methods for sample extraction. SPME has several advantages over SPE when the analysis is performed by GC-MS, since less sample volume is required; it is solvent-free and easily automated, which allows high enrichment factors in the concentration of organic compounds in aqueous matrices (Rodriguez et al. (2004)). The Oasis HLB sorbent (polystyrene-divinylbenzene-N-vinylpyrrolidone terpolymer), which exhibits both hydrophilic and lipophilic retention characteristics, has often been used for simultaneous extraction of neutral and acidic pharmaceutical residues. This materials has excellent wetting properties, thus providing the advantage of no negative *running dry* effects on the analyte recovery. Neutral and acidic compounds are retained on a solid phase by Van der Waals and H-donor-H-acceptor interactions. The less common SPE cartridges employed are RP-C18, Lichrolut ENV+, Oasis MCX and StrataX that generally need pH adjustment and sometimes special elution conditions. When performing a single group analysis, molecularly imprinted polymers (MIPs) and immunosorbents could be useful tools to provide high selectivity for target analytes. In a recent study by Gros et al. (2006), MIPs provided lower detection limits for waste water analysis than Oasis HLB, due to their specificity for target β-blockers and closely related compounds (Radjenovic (2009)).

A.2. Analytical techniques

Liquid chromatography-mass spectrometry (LC-MS, or alternatively HPLC-MS) is an analytical chemistry technique that combines the physical separation capabilities

of liquid chromatography (or HPLC) with the mass analysis capabilities of mass spectrometry.

LC-MS is a powerful technique used for many applications, which has very high sensitivity and specificity.

Liquid chromatography combined with mass spectrometry (LC-MS) and related techniques, such as ultra performance LC-MS (UPLC-MS), have become robust, sensitive techniques for detecting parent compounds at ultra-trace levels in environmental samples.

Unlike, gas chromatography (GC)-MS, LC-MS can determine polar analytes without need for previous derivatization. This advantage of LC-MS, is particularly attractive when simultaneously analysing compounds belonging to structurally distinct groups whose determination by GC-MS would involve more than one derivatization reaction.

With the advent and availability of recent analytical instrumentation that aids compound identification [e.g., LC coupled to ion-trap (IT)-MS or time-of-flight (ToF)-MS], more degradates and metabolites are being identified. These two MS techniques, provide complementary data that facilitate structural elucidation of unknown compounds. For example, the ability to conduct multiple stages of fragmentation in an IT-MS system can generate spectra with considerable amounts of structural information, that identifies an unknown degradate. Further confirmation of the proposed identity or chemical formula of new degradation products, can be achieved by accurate mass measurements using a ToF-MS system or other high resolution mass analyzers. Current bench top ToF-MS instruments, can now achieve a low femtomole (fmol)-level sensitivity, high resolving power and mass accuracy. Even more powerful in terms of confirmatory analysis are hybrid triple-quadrupole ToF-MS (QqToF-MS) systems that acquire product ion spectra with accurate mass measurements of product ions (precision in the low ppm range). An alternative to ToF instruments is the recently launched LTQ Orbitrap that combines a conventional linear IT (LIT-MS) with an Orbitrap mass analyzer. This system provides outstanding mass accuracy, mass resolution and reliable high sensitivity MSn performance.

Using LC-MS, there has been a vast number of analytical methods for determina-

tion of emerging pollutants and studies of their occurrence in the environment published (e.g., pharmaceuticals, hormones, endocrine-disrupting compounds, PFCs, drinking-water DBPs, sunscreens and ultraviolet (UV) filters, brominated flame retardants and benzotriazoles).

Recently, several articles focused on degradation products of emerging products and their toxicological effects. In this sense, in recent years, different review papers have been published on analytical methods for emerging contaminants, and the occurrence of these compounds in the environment. However, this is the first review article devoted to the fate and the ecotoxicology of emerging pollutants and especially focusing on their metabolites and TPs in the aquatic environment (Farre et al. (2008)).

The efforts to develop and refine an interface for introducing a flowing liquid high performance liquid chromatography (HPLC) system into a high vacuum mass spectrometry environment, were fueled by a strong notion, that combination would be unique and would provide powerful advantages for analysis.

From an applications standpoint, the partnership of HPLC and mass spectrometry benefited greatly from the tradition of HPLC, within the pharmaceutical industry and from the growing trend, to obtain structural and quantitative information during earlier stages of drug development. Ultimately, it has been the power of HPLC to resolve, and the ability of mass spectrometry to identify that enabled LC-MS to integrate effectively with drug development and to solve problems.

The integrated LC-MS format provides the pharmaceutical industry with a highly efficient platform to conduct a series of online steps to purify the sample and amplify the signal (Lee (2002)).

A.2.1. Samples preparations

Water samples were filtered through 1 μm glass fiber filters followed by 0.45 μm nylon membrane filters water samples were spiked, prior to the extraction, with appropriate concentrations of standard mixtures containing target analytes. For the preconcentration of water samples, a Baker vacuum system (J.T. Baker, The Netherlands) was used. In all cases, 500 mL of surface waters, 200 mL of effluent, and 100 mL of influent wastewaterswere loaded onto the cartridges at a flow rate of

approximately 5 mL min^{-1}.

All standards used were of high purity grade (>90%). Isotopically labelled compounds, used as internal standards, were 13Cphenacetin, fluoxetine - d5 and flumequine from Sigma - Aldrich (Steinham, Germany), sulfathiazole - d4 from Toronto Research Chemicals, diazepam - d5 and phenobarbital - d5 from Cerilliant (Texas, USA), atenolol - d7, carba - mazepine - d10, ibuprofen - d3 from CDN isotopes (Quebec, CAN) and mecoprop - d3 from Dr. Ehrenstorfer (Augsburg, Germany). Both individual stock standard and isotopically labelled internal standard solutions were prepared on a weight basis in methanol, except fluoroquinolones, which were dissolved in water: methanol mixture (1:1) containing 0.2% v/v hydrochloric acid (Golet et al. (2002)). After preparation, standards were stored at -20 ^{o}C. Fresh stock solutions of antibiotics were prepared monthly due to their limited stability while stock solutions for the rest of substances was renewed every three months. A mixture of all pharmaceuticals was prepared by appropriate dilution of individual stock solutions in methanol-water (25:75, v/v). Working standard solutions, also prepared in methanol-water (25:75, v/v) mixture, were renewed before each analytical run. A separate mixture of isotopically labelled internal standards, used for internal standard calibration, was prepared in methanol and further dilutions also in methanol-water (25:75, v/v) mixture.

A.2.2. HPLC-MS analysis

LC analysis was performer using an Agilent HP 1100 HPLC (Palo Alto, CA, U.S.A.), equipped with an autosampler and connected in series with a 4000 QTRAP hybrid triple quadrupole-linear ion trap mass spectrometer equipped with a Turbo Ion Spray source (Applied Biosystems-Sciex, Foster City, CA, U.S.A.). Chromatographic separation was achieved with a Purospher Star RP-18 endcapped column (125 mm 0 2.0 mm, particle size 5 μm) preceded by a C18 guard column (4 x 4, 5 μm), both supplied by Merck (Darmstadt, Germany). For the analysis in NI mode, eluent A was a mixture of acetonitrile/methanol (1:1, v/v) and eluent B was HPLC grade water at a flow rate of 0.2 mL/min. The elution gradient started with 20% eluent A, increasing to 80% in 20 min, raising to 90% in 4 min and then, back to initial conditions within 3 min. The column was re-equilibrated for 15 min before

another injection with a total time for chromatographic analysis of 42 min. The analysis in PI mode was performed using aceto nitrile as eluent A and HPLC grade water with 0.1% formic acid as eluent B. The elution gradient started with 5% eluent A, increasing to 95% in 25 min, raising to 100% in the following 5 min. Initial conditions were reached in 5 min and reequilibration time was 10 min. Chromatographic analysis lasted 45 min.

The sample injection volume was set at 20 μL in all chromatographic methods. The optimization of compound dependent MS parameters (declustering potential (DP), entrance potential (EP), collision energy (CE) and cell exit potential (CXP)) for each transition was performed by infusing standards of each individual compound at 100 μg L^{-1} to the mass spectrometer. It should be remarked that all transitions were recorded in one single retention time window, without losing sensitivity, setting appropriate values for the dwell time and pause between mass ranges. Therefore, a value of 10 (PI) and 50 ms (NI) was set for dwell time, and 2 (PI) and 5 ms (NI) for the pause between mass ranges (Gros et al. (2009), Gros et al. (2010)).

Given the polar nature of pharmaceuticals, LC-MS was the analytical method of choice (Gros et al. (2006)). All analyses were performed in the ESI+ and ESI- mode, depending on the nature of the predominant charge carrier of a certain compound in the solution. The ESI cone-jet interface involves application of a high electrical potential to a liquid sample flowing through a capillary, evaporating it and transmitting the single solvated gas phase ions to the inlet aperture of the MS for separation based on their m/z ratio, followed by detection. The LC analysis was performed using a Waters 2690 HPLC system (Milford, MA, US) coupled to a Waters Micromass Quattro QqQ-MS, equipped with a Z-spray ESI interface (Manchester, UK). Chromatographic separation was achieved with a Purospher Star RP-18 endcapped column (125mm x 2.0 mm, particle size 5μm) and a C18 guard column, both supplied by Merck (Darmstadt, Germany). For the analysis in NI mode, eluent A was methanol and eluent B was water at a flow rate of 0.2 mL min^{-1}. The elution gradient started with 20 % of eluent A, increasing to 80 % in 20 min, raising to 90 % in a 4 min gradient and then, back to initial conditions within 3 min. The column was re-equilibrated for 15 min before another injection. The analysis in PI mode was performed using as eluent A a mixture of acetonitrile-methanol (2:1) and as eluent

B a buffer consisting in NH4Ac 5 mM/HAc at pH 4.7, also at a flow rate of 0.2 mL min^{-1}. The elution gradient started with 15 % of eluent A, keeping isocratic conditions for three minutes. Then, eluent A increased to 95 % in 22 min and was held for 7 min. Finally, initial conditions were reached again in five minutes, with a re-equilibration time of 15 min in order to restore the column. The sample injection volume was set at 10 μL. MS parameters for the analysis were the following: ESI source block and desolvation temperature: 150 and 350 ^{o}C, respectively; capillary voltage: 2.8 kV; argon collision gas 2.5 x 10-3 mbar; cone nitrogen and desolvation gas flow: 43 and 636 L h^{-1}. After the selection of the precursor ions for each analyte, product ions were obtained with a combination of collision energies and cone voltages, parameters that were previously optimized. Instrument control, peak detection and integration were carried out using Masslynx NT software (version 3.4). For increased sensitivity and selectivity, data acquisition was performed working in MRM.

To confirm the presence of a compound in environmental samples when using LC-MS two transitions between precursor and product ions should be monitored working in MRM, earning 4 IPs. Other criteria used are the MRM ratio (calculated as the ratio between the abundances of both transitions) and the LC retention time. If there is poor fragmentation of some compounds, their confirmation can be performed by matching their LC retention times with the ones obtained in standards (Gros et al. (2006), Gros et al. (2009), Gros et al. (2010)). This shift between compared retention times should not exceed 2.5% in order to consider the confirmation accurate enough. In the method optimized by Gros et al. (2006) and Gros et al. (2009) transitions between a precursor ion and the two most abundant fragment ions, were chosen for each analyte when working in MRM mode, earning 4 identification points (IPs), enough to accomplish the EU directive aforementioned. In the cases where compounds showed poor fragmentation only one transition could be monitored. However, it only happened for five compounds (ibuprofen, gemfibrozil, pravastatin, ofloxacin and glibenclamide), and since the shifts in their LC renetion times in the samples and standards was less than 2 %, confirmation was considered accurate enough. For internal standards, only one transition was selected, as they are isotopically labelled compounds which are not likely to be found in environmen-

tal samples.

From table A.1 to table A.7 are reported the physico-chemical proprieties of the 73 analysed compounds (data obtained from EPIsuite v4.00, Ternes and Joss (2006), Petrovic and Barcelo (2007)). In particular in those tables the letter A...L means:

A	=	Analgesics / anti-inflammatories	G	=	Beta-blockers
B	=	Antibiotics	H	=	Diuretic
C	=	Antidiabetic	I	=	Lipid regulator
D	=	Antihypertensive	J	=	Psichiatric drugs
E	=	Barbitures	K	=	Receptor antagonist
F	=	Beta-agonists	L	=	Antineoplastic

These data are from Jelicic and Ahel (2003); Roberts and Thomas (2006); Radjenovic et al. (2009); Kasprzyk-Hordern et al. (2009); Rosal et al. (2010); Sipma et al. (2010); Sui et al. (2010); Verlicchi et al. (2010a)

Table A.1.: Physico-chemical properties of the 73 investigated PhCs

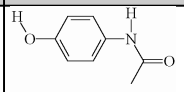
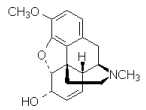
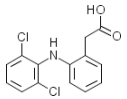
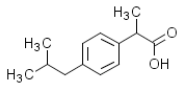
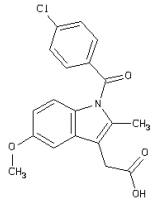
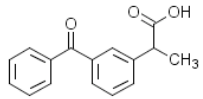
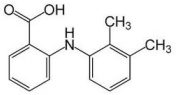
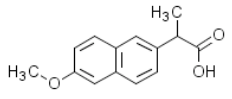
	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
A	**Acetaminophen** Analgesic; antipyretic CAS # 103-90-2	C8H9NO2	9.38	0.46		3.035 10^4		0.96-485
A	**Codeine** Analgesic (narcotic) CAS # 76-57-3	C18H21NO3	8.21	1.19	2.845	1.21 10^4		1.73-35
A	**Diclofenac** Anti-inflammatory, CAS # 15307-86-5	C14H11Cl2NO2	4.15	4.51/0.7	2.607	4.52		0.01-28
A	**Ibuprofen** Anti-inflam., analgesic, antipyretic CAS # 15687-27-1	C13H18O2	4.91	3.97/0.45	2.596	41.05		0.01-31.3
A	**Indomethacin** Anti-inflammatory, analgesic, antipyretic CAS # 53-86-1	C19H16ClNO4	4.5	4.27	2.904	3.114		0.1-1
A	**Ketoprofen** Anti-inflammatory, analgesic, CAS # 22071-15-4	C16H14O3	4.45	3.12/-0.44	2.459	120.4		0.01-3
A	**Mefenamic acid** Anti-inflammatory, analgesic, CAS # 61-68-7	C15H15NO2	4.2	5.12	2.409	1.121		0.02-25
A	**Naproxen** Anti-inflamm., analgesic, antipyretic CAS # 22204-53-1	C14H14O3	4.15	3.18/-0.34	2.543	144.9		0.02-19

Table A.2.: Physico-chemical properties of the 73 investigated PhCs

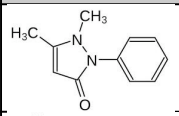
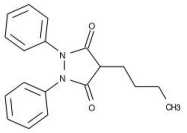
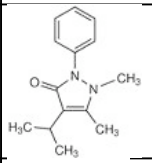
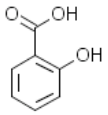
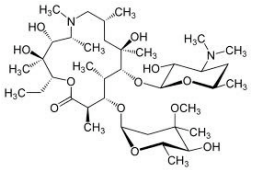
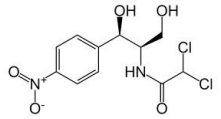
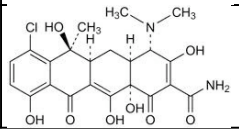
	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
A	**Phenazone** Analgesic CAS # 60-80-0	C11H12N2O	1.4	0.38	2.116	2.376 10^4		0.1-0.24
A	**Phenylbutazone** Anti-inflammatory CAS # 50-33-9	C19H20N2O2	4.5	3.16	3.357	21.95		
A	**Propyphenazone** Analgesic, antipyretic anti-inflammatory CAS # 479-92-5	C14H18N2O	---	1.96	2.814	668.2		0.04-0.46
A	**Salicylic acid** Anti-inflammatory, analgesic, antipyretic CAS # 69-72-7	C7H6O3	2.97	2.26/-2.42	1.379	3808		0.1-72.4
B	**Azithromycin** Macrolide antibiotic CAS # 83905-01-5	C38H72N2O12	pK_1 =8.7 pK_2= 9.5	4.02	3.496	0.06204		0.09-0.3
B	**Chloramphenicol** Fenicole antibiotic CAS # 56-75-7	C11H12Cl2N2O5	5.5	1.14	1.115	388.5		0.004-0.319
B	**Chlortetracycline** Tetracycline antibiotic CAS # 57-62-5	C22H23ClN2O8	pK_1= 3.3 pK_2= 7.4 pK_3= 9.3	-0.62	1.858	615.7		

Table A.3.: Physico-chemical properties of the 73 investigated PhCs

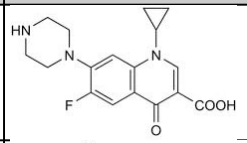
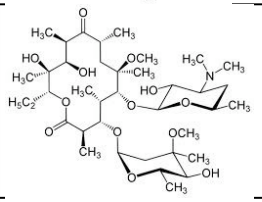
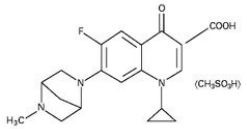
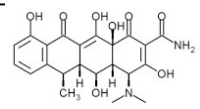
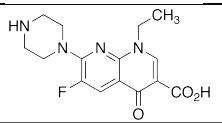
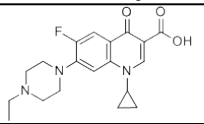
	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
B	**Ciprofloxacin** Fluoroquinolone antibiotic CAS # 85721-33-1	C17H18FN3O3	6.09	0.28	1.0	1.148 10^4		0.01-5.9
B	**Clarithromycin** Macrolide antibiotic CAS # 81103-11-9	C38H69NO13	8.99	3.16	2.174	0.342		0.16-4.82
B	**Danofloxacin** Fluoroquinolone antibiotic CAS # 112398-08-0	C19H20FN3O3	pK_1= 5.6 pK_2= 8.6	--				0.04-2.7
B	**Doxycycline** Tetracycline antibiotic CAS # 564-25-0	C22H24N2O8	pK_1= 3.5 pK_2= 7.7 pK_3= 9.5	-0.02	1.693	312.9		
B	**Enoxacin** Fluoroquinolone antibiotic CAS # 74011-58-8	C15H17FN4O3	pK_1= 6.3 pK_2= 8.7	-0.2	1.0	3.43 10^4		
B	**Enrofloxacin** Fluoroquinolone antibiotic CAS # 93106-60-6	C19H22FN3O3	pK_1= 5.9-6.3 pK_2= 7.7-8.0	-1.6-1.1; 0.70	1.174	3397		0.007-0.85

Table A.4.: Physico-chemical properties of the 73 investigated PhCs

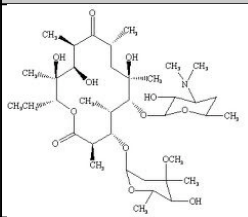
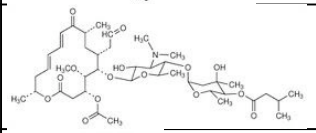
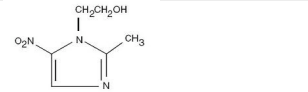
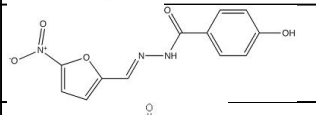
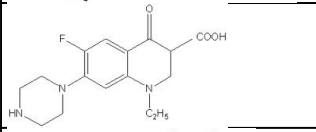
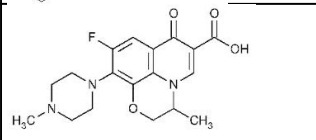
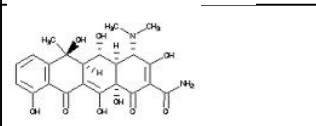
	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
B	**Erythromycin** Macrolide antibiotic CAS # 114-07-8	C37H67NO13	8.8-8.9	3.06	2.754	0.5168		0.14-10
B	**Josamycin** Macrolide antibiotic CAS # 16846-24-5	C42H69NO15		3.16, 2.39	2.938	0.4498		
B	**Metronidazole** Nitrimidazole antibiotic CAS # 443-48-1	C6H9N3O3	2.5	-0.1; -0.02	1.149	$2.573\ 10^4$		0.158-1.583
B	**Nifuroxazide** Nitrofuran antibiotic CAS # 965-52-6	C12H9N3O5		1.49	3.393	1416		
B	**Norfloxacin** Fluoroquinolone Antibiotic CAS # 70458-96-7	C16H18FN3O3	pK_1= 6.3, pK_2= 8.4	-1.03	1.271	$1.779\ 10^5$		0.01-0.96
B	**Ofloxacin** Fluoroquinolone antibiotic CAS # 82419-36-1	C18H20FN3O4	pK_1= 6.0 pK_2= 8.2	-0.39	1.086	$2.826\ 10^4$		0.01-31.7
B	**Oxytetracycline** Tetracycline antibiotic CAS # 79-57-2	C22H24N2O9	pK_1= 3.27 pK_2= 7.3 pK_3= 9.1	-0.90; -1.6 (pH 7.5) 1.22	1.867	1399		

Table A.5.: Physico-chemical properties of the 73 investigated PhCs

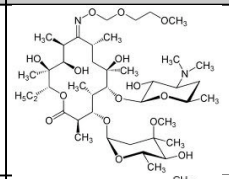
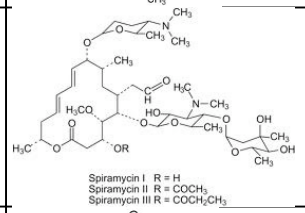
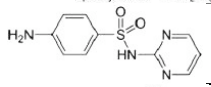
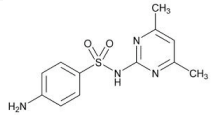
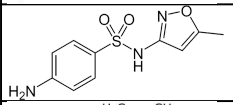
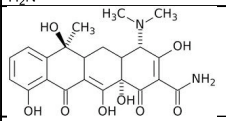
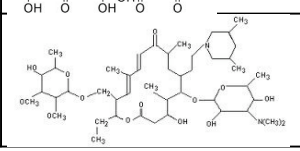
	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
B	**Roxithromycin** Macrolide antibiotic CAS # 80214-83-1	C41H76N2O15	8.8	2.75	3.984	0.01887		0.01-1
B	**Spiramycin** Macrolide antibiotic CAS # 8025-81-8	C43H74N2O14	8.0					
B	**Sulfadiazine** Sulfonamide antibiotic CAS # 68-35-9	C10H10N4O2S	pK_1= 6.36 pK_2= 2.1	-0.09	1.871	2.814 10^4		0.002-0.022
B	**Sulfamethazine** Sulfonamide antibiotic CAS # 57-68-1	C12H14N4O2S	pK_1= 7.59 pK_2= 2..3	0.19	2.282	1.124 10^4		
B	**Sulfamethoxazole** Sulfonamide antibiotic CAS # 723-46-6	C10H11N3O3S	pK_1= 5.7 pK_2= 1.8	0.89	2.412	3942		0.01-6
B	**Tetracycline** Tetracycline antibiotic CAS # 60-54-8	C22H24N2O8	pK_1= 3.3 pK_2= 7.7 pK_3= 9.7	-1.30	1.644	3877		0.01-1.3
B	**Tilmicosin** Macrolide antibiotic CAS # 108050-54-0	C46H80N2O13	8.18	3.80	4.039	0.01481		

Table A.6.: Physico-chemical properties of the 73 investigated PhCs

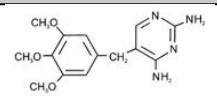
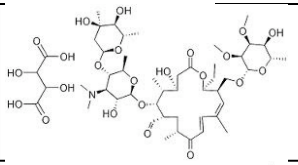
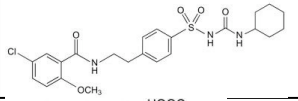
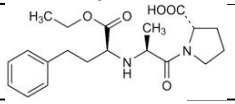
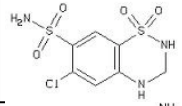
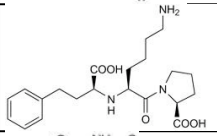
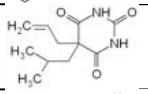
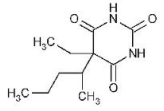
	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
B	**Trimethoprim** Diaminopyrimidine CAS # 738-70-5	C14H18N4O3	7.2	0.91	2.857	2334		0.02-6.8
B	**Tylosin A** Macrolide antibiotic CAS # 1401-69-0	C46H77NO17	7.73	1.63	2.873	0.5065		
C	**Glibenclamide** Anti-diabetic CAS # 10238-21-8	C23H28ClN3O5S	5.3	4.8	3.166	0.0635		0.05-15.9
D	**Enalapril** Antihypertensive CAS # 75847-73-3	C20H28N2O5	---	2.45	2.542	34.88		
D	**Hydrochlorothiazide** Antihypertensive CAS # 58-93-5	C7H8ClN3O4S2	7.9	-0.07	1.078	1292		
D	**Lisinopril** Antihypertensive CAS # 83915-83-7	C21H31N3O5	2.5	-1.22	4.148	8.6		
E	**Butalbital** Barbiturate CAS # 77-27-9	C11H16N2O3	---	1.87	1.408	829.7		
E	**Pentobarbital** Barbiturate CAS #76-74-4	C11H18N2O3	8.11	2.10	1.442	512.8		

Table A.7.: Physico-chemical properties of the 73 investigated PhCs

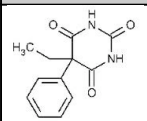
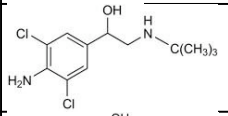
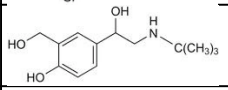
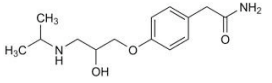
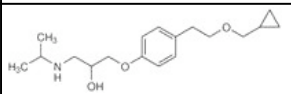
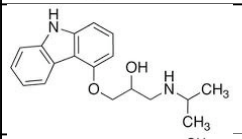
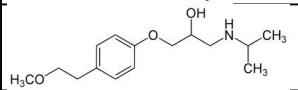
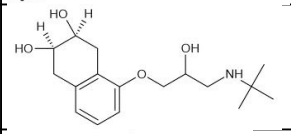
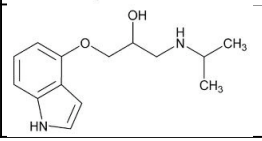
	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
E	**Phenobarbital** Barbiturate CAS # 50-06-6	C12H12N2O3	7.3	1.47	1.767	1644		0.07
F	**Clenbuterol** Beta-agonist CAS # 037148-27-9	C12H18Cl2N2O	---	2.00	3.174	3320		
F	**Salbutamol** Beta-agonist CAS # 35763-26-9	C13H21NO3	pK_1= 9.3, pK_2=10.3	0.6, 0.01	--	--		
G	**Atenolol** Beta-blocker CAS # 29133-68-7	C14H22N2O3	9.6	0.16	1.825	685.2		0.15-33.1
G	**Betaxolol** Beta-blocker CAS # 63659-18-7	C18H29NO3	---	2.81	2.848	450.7		
G	**Carazolol** Beta-blocker CAS #57775-29-8	C18H22N2O2	---	3.59	3.728	8.254		
G	**Metoprolol** Beta-blocker CAS # 37350-58-6	C15H25NO3	9.6	1.88	2.057	4777		0.03-1539
G	**Nadolol** Beta-blocker CAS # 42200-33-9	C17H27NO4	9.67	0.81	2.208	2.24 10^4		
G	**Pindolol** Beta-blocker CAS # 13523-86-9	C14H20N2O2	9.25	1.75	2.694	7883		

Table A.8.: Physico-chemical properties of the 73 investigated PhCs

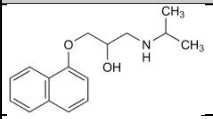
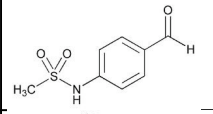
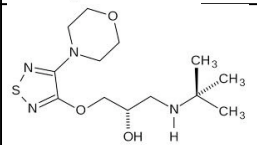
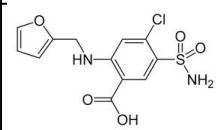
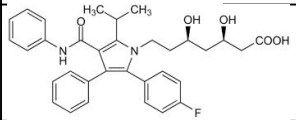
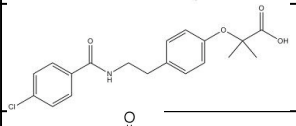
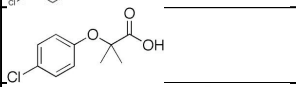
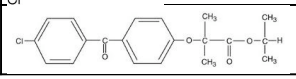
	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
G	**Propranolol** Beta-blocker CAS # 525-66-6	C16H21NO2	9.42	3.48	2.955	228		0.11-8.9
G	**Sotalol** Beta-blocker CAS # 3930-20-9	C12H20N2O3S	pK_1=8.2 pK_2=9.8	0.24	1.351	5513		0.17-3.3
G	**Timolol** Beta-blocker CAS # 26839-75-8	C13H24N4O3S	9.21	1.83	1	2741		
H	**Furosemide** Diuretic CAS # 54-31-9	C12H11ClN2O5S	3.9	2.03	2.043	149.3		0.84-6
I	**Atorvastatin** Lipid regulator CAS # 134523-00-5	C33H35FN2O5		6.36	4.456	0.001115		0.05-0.16
I	**Bezafibrate** Lipid regulator CAS # 41859-67-0	C19H20ClNO4	3.60	4.25	2.617	1.224		0.07-30
I	**Clofibric acid** Lipid regulator CAS # 882-09-7	C10H11O3	---	2.57	1.640	582.5		0.02-1.2
I	**Fenofibrate** Lipid regulator CAS # 49562-28-9	C20H21ClO4	---	5.19	3.587	0.1957		

Table A.9.: Physico-chemical properties of the 73 investigated PhCs

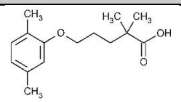
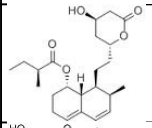
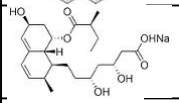
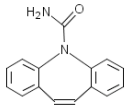
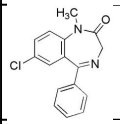
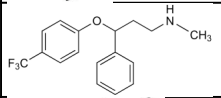
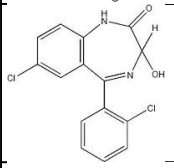
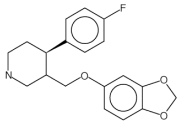
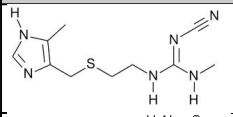
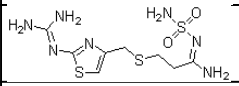
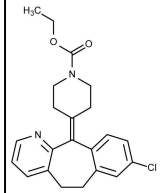
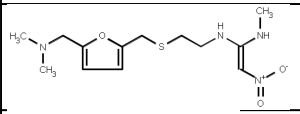
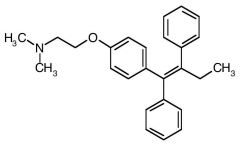
	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
I	**Gemfibrozil** Lipid regulator CAS # 25812-30-0	C15H2203	4.8	4.77	2.636	4.964		0.12-36.5
I	**Mevastatin** Lipid regulator CAS # 73573-88-3	C23H34O5	---	3.95	3.665	4.801		
I	**Pravastatin** Lipid regulator CAS # 81093-37-0	C23H36O7	---	-0.23	2.401	2464		0.06-1.50
J	**Carbamazepine** Psychiatric drug CAS # 298-46-4	C15H12N2O	13.9	2.45	3.123	17.66		0.02-29.3
J	**Diazepam** Psychiatric drug CAS # 439-14-5	C16H13ClN2O	3.4	2.82	3.875	58.78		
J	**Fluoxetine** Psychiatric drug CAS # 54910-89-3	C17H18F3NO	9.5	4.05	4.971	38.35		
J	**Lorazepam** Psychiatric drug CAS # 846-49-1	C15H10Cl2N2O2	pK_1=1.3 pK_2=11.5	2.39	2.975	83.87		
J	**Paroxetine** Psychiatric drug CAS # 61869-08-7	C19H20FNO3	9.0	3.95	4.092	35.27		0.04-0.06

Table A.10.: Physico-chemical properties of the 73 investigated PhCs

	Pharmaceutical	Formula	pK_a	log K_{ow}	log K_{oc}	S_w 25°C (mg l^{-1})	Molecular structure	Observed Range (g L^{-1})
K	**Cimetidine** Receptor antagonist CAS # 51481-61-9	C10H16N6S	6.8	0.40	2.798	1.046 10^4		0.7-13.057
K	**Famotidine** Receptor antagonist CAS # 76824-35-6	C8H15N7O2S3	---	-0.64	3.491	1271		0.03-0.14
K	**Loratadine** Receptor antagonist CAS # 79794-75-5	C22H23ClN2O2	---	5.20	5.771	0.01099		0.02-0.04
K	**Ranitidine** Receptor antagonist CAS # 66357-35-5	C13H22N4O3S	2.4	0.27	3.839	2.466 10^4		0.01-11.7
L	**Tamoxifen** antineoplastic CAS # 10540-29-1	C26H29NO		6.30	6.417	0.1936		0.143-0.215

Another important table referring to the optimized QqLIT-MS/MS parameters by SRM Negative and Positive Ionization Mode and all those data are reported in table A.11 for the negative ionization mode and in table A.12 for the positive ionization mode.

Table A.11.: Target Compounds and Their Optimized QqLIT-MS/MS Parameters by SRM Negative Ionization Mode

Compounds	precursor ion (m/z)	SRM 1	Collision Energy 1	SRM 2	Collision Energy 2	Rt (min)	IS used for quantification
Acetaminophen	150	107	22			3.6	mecoprop-d3
Salicylic acid	137	93	20	66	38	4.1	mecoprop-d3
Hydrochlorothiazide	296	78	28			6.1	mecoprop-d3
Clofibric acid	213	127	26	85	14	12.9	mecoprop-d3
Furosemide	329	205	22	285	32	13.3	ibuprofen-d3
Naproxen	229	185	10	169	38	14.3	mecoprop-d3
Mecoprop-d3 (IS)	218	146	24			14.8	
Ketoprofen	253	209	12	197	6	14.9	mecoprop-d3
Phenobarbital-d5 (IS)	236	193	16			14.2	
Phenobarbital	231	188	14			14.2	phenobarbital-d5
Chloramphenicol	323	152	22	194	18	15.1	ibuprofen-d3
Butalbital	223	180	16	85	18	16.6	ibuprofen-d3
Bezafibrate	360	274	26	154	38	16.7	ibuprofen-d3
Pentobarbital	225	182	18	85	18	18.6	ibuprofen-d3
Ibuprofen-d3 (IS)	208	164	10			19.1	
Ibuprofen	205	161	10			19.2	ibuprofen-d3
Diclofenac	294	250	16	214	30	19.9	ibuprofen-d3
Indomethacine	356	312	12	297	24	20.6	ibuprofen-d3
Mefenamic acid	240	196	20	180	38	21.1	ibuprofen-d3
Gemfibrozil	249	121	20	127	14	24.3	ibuprofen-d3

A.3. La Spezia analysis

All the water analysis in the WWs derived from the experimental investigation in La Spezia were analysed in the Department of Environmental Health Science Mario Negri Institute for Pharmacological Research in Milan by Professor Zuccato and his work team with the method reported below and also explained in Zuccato et al. (2010)

Standards were dissolved in methanol to a concentration of 1mg mL^{-1} and subsequently diluted to 10 ng μL^{-1} (stock solution) and 1-0.1 ng μL^{-1} (working solutions). The stock solutions of amoxicillin, ciprofloxacin, ofloxacin, oxytetracycline and sulphamethoxazole were renewed monthly because of their limited stability. The I.S. were dissolved in methanol (1 mg mL^{-1}) and subsequently diluted to 10 and 1 ng μL^{-1}. All stock and I.S. solutions were stored at -20 ^{O}C in the dark.

The cartridges used for solid phase extraction were: 3 mL disposable OASIS MCX

Table A.12.: Target Compounds and Their Optimized QqLIT-MS/MS Parameters by SRM Positive Ionization Mode

Compounds	precursor ion (m/z)	SRM 1	Collision Energy 1	SRM 2	Collision Energy 2	Rt (min)	IS used for quantification
Salbutamol	240	148	25	166	20	5.7	atenolol-d7
Metronidazole	172	172	21	82	37	5.8	13C-Phenacetin
Sotalol	273	213	25	255	25	6.1	atenolol-d7
Atenolol	267	145	35	190	35	6.2	atenolol-d7
Atenolol-d7 (IS)	274	145	37			6.2	
Cimetidine	253	95	30	159	23	6.3	atenolol-d7
Famotidine	338	189	27	259	20	6.3	atenolol-d7
Ranitidine	315	176	25	130	39	6.5	atenolol-d7
Sulfadiazine	253	156	25	92	43	7.3	sulfathiazol-d4
Codeine	300	152	85	115	105	7.4	
Lisinopril	406	84	75			8.1	atenolol-d7
Sulfathiazol-d4 (IS)	260	160	23			8.2	
Nadolol	310	254	30	201	35	8.5	atenolol-d7
Trimethoprim	291	230	33	261	31	8.8	
Pindolol	249	116	30	98	30	8.8	atenolol-d7
Enoxacin	321	303	30	234	33	8.9	flumequine
Ooxacin	362	261	39			9.2	flumequine
Oxytetracycline	461	426	25	201	51	9.2	13C-Phenacetin
Norfloxacin	320	302	35			9.3	flumequine
Ciprooxacin	332	288	25	231	51	9.4	flumequine
Sulfamethazine	279	186	25	124	33	9.5	sulfathiazol-d4
Danooxacin	358	340	35	314	27	9.7	flumequine
Doxycycline	445	410	29	154	41	9.7	13C-Phenacetin
Phenazone	189	56	40	147	33	9.8	carbamazepine-d10
Timolol	317	261	30	244	30	9.8	atenolol-d7
Enrofloxacin	360	316	29	245	39	9.9	flumequine
Metoprolol	268	121	35	133	35	10.2	atenolol-d7
Clenbuterol	277	203	23	132	33	10.3	atenolol-d7
Spiramycin	843	174	53	540	43	10.7	carbamazepine-d10
Azithromycin	749	591	43	573	50	10.9	carbamazepine-d10
Chlortetracycline	479	462	29	444	29	11.4	13C-Phenacetin
Carazolol	299	116	35	222	35	11.8	atenolol-d7
Tetracycline	445	428	20			11.8	13C-Phenacetin
Tilmicosin	869	696	61	174	55	11.8	carbamazepine-d10
Sulfamethoxazole	254	156	25	92	41	12.5	sulfathiazol-d4
Enalapril	377	234	29	303	35	12.5	diazepam-d5
Propranolol	260	116	35	183	30	12.5	atenolol-d7
13C-Phenacetin (IS)	181	139	23			12.7	
Nifuroxazide	276	121	25	65	73	12.8	13C-Phenacetin
Betaxolol	308	116	40	121	40	12.9	atenolol-d7
Erithromycin	734	158	41	576	35	13.4	carbamazepine-d10
Tylosin A	916	174	63	773	41	14.1	carbamazepine-d10
Pravastatin	447	327	29			14.2	carbamazepine-d10
Paroxetine	330	192	31	123	45	14.4	fluoxetine-d5
Carbamazepine-d10 (IS)	247	204	31			14.5	
Clarithromycin	748	591	35	158	40	14.6	carbamazepine-d10
Carbamazepine	237	194	29			14.7	carbamazepine-d10
Roxithromycin	838	158	49	679	31	15.1	carbamazepine-d10
Fluoxetine	310	44	93	148	13	15.1	fluoxetine-d5
Fluoxetine-d5 (IS)	315	153	13			15.3	
Propyphenazone	231	56	57	189	35	15.3	carbamazepine-d10
Flumequine (IS)	262	202	47			15.4	
Josamycin	828	174	45	600	37	15.6	carbamazepine-d10
Lorazepam	323	174	45	229	45	15.7	diazepam-d5
Loratadine	383	337	33	267	47	17.5	carbamazepine-d10
Diazepam	285	193	45	154	50	17.6	diazepam-d5
Diazepam-d5 (IS)	290	198	43			17.6	
Tamoxifen	372	72	43	327	35	19.4	carbamazepine-d10
Atorvastatin	559	440	27	250	63	19.8	carbamazepine-d10
Glibenclamide	494	369	23	169	55	20.7	carbamazepine-d10
Phenylbutazone	309	77	77	160	29	20.7	carbamazepine-d10
Mevastatin	391	185	19	159	39	21.5	carbamazepine-d10
Fenofibrate	361	139	43			25.2	diazepam-d5

(60 mg, Waters Corp., Milford, MA) and 3 mL disposable Lichrolut EN (200 mg, Merck, Darmstadt, Germany). All the solvents were of reagent grade or higher. Acetone, methanol, ethyl acetate were for pesticide analysis (Carlo Erba Reagents, Italy), acetonitrile for LC-MS (Riedel de Haen, Seelze, Germany). Ammonium hydroxide solution (25%), formic acid (98-100%) and triethylamine (99.5%) were from Fluka (Steinheim, Germany). Hydrochloric acid (37%) was from Carlo Erba (Milan, Italy). HPLC grade Milli-Q water was obtained with a MILLI-RO PLUS 90 apparatus (MILLIPORE, Molshelm, France).

A.3.1. Solid phase extraction

Waste and surface water samples were extracted as described in Castiglioni et al. (2006), where detailed information on recoveries and performance of the methods are reported. Briefly, water samples were filtered on glass microfiber filters GF/A 1.6 μm (Whatman, Kent, UK) and spiked with internal standards before extraction. The extraction was done on two SPE columns, an Oasis MCX at pH 2.0 for amoxicillin, ciprofloxacin, l-floxacin/ofloxacin, lincomycin, sulphamethoxazole, vancomycin, oleandomycin, oxytetracycline and tilmicosin, and a Lichrolut EN at pH 7.0 for clarithromycin, erythromycin, erythromycin-H_2O, spiramycin and tylosin. Wastewater and river water samples, respectively 50 and 500 mL aliquots, were spiked with 20 ng of internal standards (salbutamol-D_3 and ibuprofen-D_3). The Oasis MCX cartridges were conditioned before use with 6 mL methanol, 3 mL Milli-Q water and 3 mL water acidified to pH 2. Samples were then passed through the cartridges under vacuum, and the cartridges were vacuum-dried for 5 min. Elution was with 3 mL methanol, and 3 mL 2% ammonia solution in methanol. The Lichrolut EN cartridges were conditioned before use with 6 mL methanol and 6 mL Milli-Q water. Cartridges were vacuum-dried for 10 min and eluted with 3 mL methanol and 3 mL ethyl acetate. All the eluates were pooled and dried under a nitrogen stream. An ultrasonic solvent extraction (USE) was used for sludge samples extraction as previously described for particulate (Castiglioni et al. (2006)). Sludge (5 g) was extracted three times with 20 mL methanol, and after each extraction step, the samples were centrifuged for 10 min at 6000 rpm. The supernatants were finally pooled, dried under an air stream, redissolved in 100 μL Milli-Q water and

filtered before analysis. The instrumental limits of quantification (IQL) were in the hundreds pg/injected range, and the limits of quantification (LOQ) of the method were in the low ng L^{-1} range (0.5-2 ng L^{-1}).

A.3.2. HPLC-MS-MS analysis

Samples were analysed by reversed-phase liquid chromatography-tandem mass spectrometry (HPLC-MS-MS). Samples were analysed with an HPLC system consisting of two Perkin-Elmer Series 200 pumps and a Perkin-Elmer Series 200 auto sampler, and an API 3000 triple quadrupole (Q1q2Q3) mass spectrometer equipped with a turbo ion spray source (Applied Biosystems-Sciex, Thornhill, Ontario, Canada). A Luna C8 column 50mm$\times$ 2mm i.d., 3 μm particle size (Phenomenex, Torrance, CA, USA) was used for chromatographic separation at a flow rate of 200 μL min^{-1}. Mass spectrometric analysis was done in the multiple reaction monitoring mode (MRM), in negative (sulphamethoxazole) and positive ionisation modes (all the other compounds). Quantification was by isotope dilution using ibuprofen-D_3 for sulphamethoxazole and salbutamol-D_3 for the other antibiotics.

APPENDIX B

Experimental campaigns carried out

This simple appendix was made in order to explain in only one table (see table B) all the experimental investigation carried out in this Ph.D. research.

In fact, more than 6 experimental investigations weredeveloped in these years of study and also in reading all the thesis perhaps some point results unclear, this may be done from the frequent overlap of the experimentation periods.

It is possible to say that all the experimental section started in the final part of 2007 with a first screening of Lagosanto HWWs. In this first experimentation mainly macroparameters were analysed in order to understand the effective nature of HWWs. In this phase also a focus on the main PhCs were done.

The subsequent step in the experimentation were obtained with the help of a lot of partners that financed and helped all the different managing aspect. I want to thank one more time all these different assistants.

Summarizing table B shown the site, the treatment step, the kind of waters and the period of observation for the general aspect of each phase. Moreover it reports all the searched and detected compounds for the PhCs analysis, all the samples analysed and the kind of sample taken. At the end of the table, the last columns shown all the partners involved in each specific research and the section where each experimentation is explained in this thesis. In order to avoid a repetition of the

different data table yet presented during the text, in this table are reported the table number and page where we find the different analytical data, referring to the specific experimentation.

Table B.1.: Experimental investigation

Site	Treatment	Water	Period	Searched	Detected	Samples	Kind of samples	Partners	Section	Table	Page
PhCs											
Po River	–	Surface	03/2010	73	27	3	Instantaneous	1, 2, 7	2.5.1	C.2	228
Ferrara, Po	–	GW	09/2009	73	36	6	Instantaneous	1, 2, 7	2.5.2	C.3	229
Ferrara wells	–	GW	03/2010	73	10	1	Instantaneous	1, 2, 7	2.5.2	C.4	231
Ferrara	Water works	Surface → DW	03/2010	73	21	5	Instantaneous	1, 2, 7	2.5.3	C.5	232
Lagosanto	Raw	HWW	08-09/2009	73	59	4	24 hours	2, 3, 7	3.6.1	C.6	233
Ferrara	Raw	HWW	09/2009 - 03/2010	73	47^{s}-57^{w}	5	24 hours	2, 3, 7	3.6.2	C.7	235
Lagosanto	Raw	HWW	05/2007- 03/2008	20	2	3	24 hours	3, 6, 7	4.2	4.5	102
Lagosanto	CAS	UWW	05/2007- 03/2008	20	2	3	24 hours	3, 6, 7	4.2	4.5	102
La Spezia	CAS	UWW	05-06/2008	38	19	3	24 hours	1, 4, 5	4.3	C.8	237
La Spezia	MBR	UWW	05-06/2008	38	21	8	24 hours	1, 4, 5	4.3	C.8	237
La Spezia	MBR + O_3	UWW	05-06/2008	38	13	1	24 hours	1, 4, 5	4.3	C.8	237
Ferrara	CAS	UWW	03/2010	73	59	4	4 hours	1, 2	4.4	C.9	238
Ferrara	CW infl.	UWW	03-04/2010	73	52	4	4 hours	1, 2	4.5	C.10	240
Ferrara	CW effl.	UWW	03-04/2010	73	42	4	4 hours	1, 2	4.5	C.11	242
Ferrara	CW infl.	UWW spiked	03-06/2010	3	3	12	4 hours	11	4.6	C.12	243
Ferrara	CW effl.	UWW spiked	03-06/2010	3	3	12	4 hours	11	4.6	C.12	243
Macroparameter											
Rimini	Disinf.	HWW	10-11/2009	A		Variable	Instantaneous	6, 8, 9	4.1	4.4	98
Lagosanto	MBR	HWW	05/2007-03/2008	B		Variable	Instantaneous	3, 6, 7, 10	4.2	4.8	110
Ferrara	CAS	UWW	2009/2010	C		Variable	Instantaneous	1	4.4	4.17	121
Ferrara	CW	UWW	2009/2010	D		Variable	Instantaneous	1	4.5	4.19	129

1 = HERA Ferrara; 2 = CSIC Barcelona; 3 = USL Ferrara; 4 = ACAM La Spezia; 5 = Mario Negri Institute; 6 = CADF Ferrara; 7 = ATO6 Ferrara; 8 = USL Rimini; 9 = Newster S.r.l.; 10 = Ser.Eco S.r.l.; 11 = Dept. of Chemistry in Ferrara

^{s} = Summer, ^{w} = Winter

A = TC, *E. coli*, SS; B = BOD_5, COD, SS, P, NH_4, Hg, Surfactant, *E. coli*; C = BOD_5, COD, SS, P, TKN, *E. coli*; D = BOD_5, COD, SS, TKN, Redox Potential, Sulphates

APPENDIX C

Analytical results on PhCs

This appendix shows all the analytical results on PhCs analysis done in the different water matrix during the experimental section. For simplicity table C.1 resumes all the kind of water where is possible to find some information about the specific topic.

Table C.1.: Summary of the total analytical data

Water	**Analytical data (page)**	**Section (page)**
Po River	C.2 (228)	2.5.1 (35)
GW	C.3 (229)	2.5.2 (37)
Wells	C.4 (231)	2.5.2 (37)
Step of Ferrara water works	C.5 (232)	2.5.3 (42)
Lagosanto HWWs	C.6 (233)	3.6.1 (81)
Ferrara HWWs	C.7 (235)	3.6.2 (84)
La Spezia WWs	C.8 (237)	4.3 (114)
Ferrara WWTP Influent	C.9 (238)	4.4 (121)
Ferrara WWTP Effluent or CW Influent	C.10 (240)	4.5 (127)
Ferrara CW Effluent	C.11 (242)	4.5 (127)

Table C.2.: Po River waters (ng L^{-1})

Compounds	**1st sample**	**2nd sample**	**3th sample**
Acetaminophen	11	11	11
Atenolol	31	28	30
Butalbital	–	–	12
Carbamazepine	31	30	28
Clenbuterol	16	18	12
Diclofenac	34	33	57
Enoxacin	26	–	16
Erithromycin	22	–	–
Hydrochlorothiazide	77	94	118
Ibuprofen	10	13	13
Lorazepam	28	24	14
Mefenamic acid	10	11	9
Metoprolol	16	18	12
Mevastatin	10	23	10
Naproxen	13	13	16
Norfloxacin	55	37	45
Paroxetine	32	16	20
Phenobarbital	14	–	23
Phenylbutazone	41	–	–
Pravastatin	25	11	27
Propyphenazone	18	–	–
Ranitidine	88	46	49
Salbutamol	15	18	12
Salicylic acid	30	41	39
Sotalol	70	80	84
Sulfadiazine	21	18	12
Sulfamethoxazole	12	10	19
Average	**29**	**28**	**29**
Sum	**756**	**593**	**688**

Table C.3.: GWs (ng L^{-1})

Compounds	**S1A**	**S1B**	**S2A**	**S2B**	**S3A**	**S3B**
Acetaminophen	34	44	28	52	49	65
Atenolol	–	–	112	–	–	22
Butalbital	42	–	–	–	–	–
Carbamazepine	–	–	–	–	34	–
Chloramphenicol	–	–	–	–	20	–
Chlortetracycline	–	–	12	15	36	41
Ciprofloxacin	–	–	–	–	–	21
Diclofenac	13	–	–	–	–	–
Doxycycline	–	–	–	85	165	149
Enoxacin	–	–	–	–	11	12
Erithromycin	15	14	20	48	10	58
Fluoxetine	31	–	12	–	21	17
Indomethacine	1983	836	611	120	615	269
Ketoprofen	374	447	397	197	547	887
Lorazepam	–	–	–	25	24	10
Mefenamic acid	162	135	88	70	103	38
Metoprolol	16	13	21	18	55	33
Metronidazole	38	36	19	13	61	64
Mevastatin	164	217	182	277	263	120
Naproxen	48	70	68	55	124	186
Nifuroxazide	11	63	24	25	23	92
Norfloxacin	10	–	–	–	–	11
Ofloxacin	11	–	13	–	17	23
Oxytetracycline	32	18	13	47	70	93
Pentobarbital	–	11	–	28	34	33
Phenobarbital	49	–	–	–	–	15
Phenylbutazone	–	11	52	–	21	20
Pravastatin	18	–	59	16	–	32
Propyphenazone	–	–	–	–	–	13
Salicylic acid	30	33	37	42	37	39
Sotalol	–	–	15	–	–	–
Sulfadiazine	–	–	–	–	13	–

Sulfamethazine	–	–	77	70	63	74
Sulfamethoxazole	–	–	–	–	10	12
Tetracycline	–	–	–	21	28	99
Timolol	–	–	–	10	21	18
Average	**162**	**139**	**93**	**62**	**92**	**86**
Sum	**3080**	**1948**	**1858**	**1233**	**2477**	**2566**

Table C.4.: Wells mixture waters (ng L^{-1})

Compounds	**Wells mixture**
Carbamazepine	46
Erithromycin	19
Hydrochlorothiazide	41
Lorazepam	19
Norfloxacin	31
Paroxetine	27
Pravastatin	11
Ranitidine	63
Salicylic acid	35
Sulfamethazine	51
Average	**34**
Sum	**344**

Table C.5.: DWs (ng L^{-1})

Compounds	**Lag.**	**Clarifl.**	**Ozon.**	**AC filtr.**	**DW**
Atenolol	23	–	–	–	–
Carbamazepine	31	24	–	–	–
Clenbuterol	30	17	–	–	–
Diclofenac	22	13	–	–	–
Enoxacin	12	10	–	–	–
Erithromycin	19	18	–	–	–
Hydrochlorothiazide	67	47	50	–	–
Ibuprofen	13	–	–	–	–
Lorazepam	17	16	11	–	–
Metoprolol	30	17	–	–	–
Naproxen	16	–	–	–	–
Norfloxacin	21	15	12	–	–
Paroxetine	28	20	19	14	14
Phenobarbital	13	11	–	–	–
Phenylbutazone	29	–	–	–	–
Pravastatin	19	–	–	–	–
Ranitidine	173	21	12	18	–
Salbutamol	15	–	–	–	–
Salicylic acid	31	32	40	44	28
Sotalol	71	62	–	–	–
Sulfamethoxazole	14	15	–	–	–
Average	**33**	**23**	**24**	**25**	**21**
Sum	**694**	**339**	**145**	**76**	**42**

Table C.6.: Lagosanto HWWs (ng L^{-1})

Compounds	**Samples**			
	1st	**2**nd	**3**th	**4**th
Acetaminophen	5906	5161	3722	3344
Atenolol	5044	3511	5767	6200
Atorvastatin	95	73	103	62
Azithromycin	11	108	–	–
Betaxolol	13	12	–	20
Bezafibrate	2944	562	221	57
Butalbital	38	15	14	–
Carbamazepine	867	659	767	641
Chlortetracycline	50	20	20	63
Cimetidine	32	26	26	19
Ciprofloxacin	10510	11862	14723	9977
Clarithromycin	38	137	38	24
Clofibric acid	43	14	–	11
Codeine	258	358	432	396
Diclofenac	457	290	301	169
Doxycycline	193	136	97	266
Enalapril	269	151	199	186
Enoxacin	434	335	395	475
Erithromycin	164	114	319	62
Famotidine	90	183	290	87
Fenofibrate	11	–	–	26
Fluoxetine	–	18	–	–
Furosemide	17667	15889	13367	10589
Gemfibrozil	19	18	18	20
Glibenclamide	69	48	97	85
Hydrochlorothiazide	1339	1409	2114	2127
Ibuprofen	1633	1526	2518	1017
Indomethacine	4064	2265	311	3199
Ketoprofen	9840	2553	5473	2240
Lisinopril	185	609	78	139
Loratadine	14	–	–	–

Lorazepam	636	621	628	789
Mefenamic acid	178	497	364	301
Metoprolol	870	864	990	581
Metronidazole	483	433	328	1642
Mevastatin	717	971	383	1961
Naproxen	1213	2122	2831	3195
Nifuroxazide	2302	98	635	2556
Norfloxacin	45	63	103	55
Ofloxacin	12948	22244	20973	18257
Oxytetracycline	889	296	621	1319
Pentobarbital	74	22	11	33
Phenobarbital	29	27	–	–
Phenylbutazone	38	10	47	54
Pindolol	263	78	112	32
Pravastatin	190	674	594	1039
Propranolol	–	40	51	–
Propyphenazone	20	12	13	–
Ranitidine	244	1750	2200	1678
Salbutamol	103	50	51	42
Salicylic acid	1244	1983	1156	897
Sotalol	3798	4689	5940	4579
Spiramycin	–	40	–	–
Sulfadiazine	33	33	34	29
Sulfamethazine	–	14	13	–
Sulfamethoxazole	3253	4250	6452	3004
Tetracycline	21	–	10	26
Tilmicosin	73	58	67	51
Trimethoprim	817	1322	1828	801
Average	**1687**	**1631**	**1918**	**1688**
Sum	**92777**	**91326**	**97842**	**84420**

Table C.7.: Ferrara HWWs (ng L^{-1})

Compounds	**Samples**				
	1st	**2**nd	**3**th	**4**th	**5**th
Acetaminophen	4658	3450	3390	1426	2793
Atenolol	2586	2208	6550	5650	5050
Atorvastatin	173	80	244	252	308
Azithromycin	46	50	577	769	1044
Bezafibrate	–	–	44	42	510
Butalbital	52	11	247	477	342
Carbamazepine	1183	758	1083	1008	748
Chlortetracycline	93	62	–	–	–
Cimetidine	–	–	37	33	265
Ciprofloxacin	1889	1379	14944	26167	23056
Clarithromycin	50	64	13500	9330	10000
Clenbuterol	–	–	1193	1108	862
Clofibric acid	–	–	12	14	–
Codeine	636	422	2080	3167	410
Diazepam	–	–	38	33	21
Diclofenac	271	176	527	527	476
Doxycycline	97	56	–	–	–
Enalapril	176	85	244	404	284
Enoxacin	105	58	189	181	448
Erithromycin	79	86	154	227	91
Famotidine	48	35	75	134	97
Fluoxetine	24	33	35	63	69
Furosemide	7717	6389	5297	6281	5719
Gemfibrozil	–	–	64	14	19
Glibenclamide	71	66	103	113	72
Hydrochlorothiazide	816	536	2331	2388	1838
Ibuprofen	813	380	3220	2419	2230
Indomethacine	895	3409	607	403	590
Ketoprofen	1417	829	1370	1765	1066
Lisinopril	337	89	–	–	–
Loratadine	–	–	20	15	26

Lorazepam	198	167	640	698	464
Mefenamic acid	104	131	748	564	331
Metoprolol	970	507	1193	1108	862
Metronidazole	392	261	958	1057	853
Mevastatin	531	449	68	189	204
Naproxen	339	485	10867	2767	1077
Nifuroxazide	158	103	334	222	326
Norfloxacin	23	44	305	224	513
Ofloxacin	4049	3262	31769	36538	24538
Oxytetracycline	74	104	–	–	–
Paroxetine	–	–	76	69	56
Pentobarbital	14	24	149	122	110
Phenobarbital	27	13	358	256	131
Phenylbutazone	48	77	123	170	118
Pindolol	–	–	48	–	42
Pravastatin	64	77	269	154	81
Propranolol	94	76	61	37	30
Propyphenazone	–	–	98	–	–
Ranitidine	1511	1077	1407	3586	4107
Roxithromycin	–	–	136	77	23
Salbutamol	27	27	99	140	123
Salicylic acid	1053	989	2413	2360	1906
Sotalol	352	613	6723	5193	3306
Spiramycin	–	–	62	108	34
Sulfadiazine	119	77	329	271	383
Sulfamethazine	–	–	27	13	30
Sulfamethoxazole	2670	900	3364	1733	936
Tilmicosin	14	16	123	318	348
Timolol	–	–	22	39	38
Trimethoprim	860	449	359	117	68
Average	**807**	**652**	**2128**	**2228**	**1809**
Sum	**37923**	**30639**	**121306**	**122541**	**99473**

Table C.8.: La Spezia WWs (ng L^{-1})

Date	**May 6**	**May 7**	**May 6**	**May 7**	**June 19**	**June 20**	**June 19**	**June 26**	**June 27**	**June 26**	**June 30**	**June 30**
Compound	**Influent MBR**	**Influent MBR**	**Effluent MBR**	**Effluent MBR**	**Influent CAS/MBR**	**Effluent CAS**	**Effluent MBR**	**Influent CAS/MBR**	**Effluent CAS**	**Effluent MBR**	**Effluent MBR**	**Effluent MBR + O_3**
Atenolol	8803	7076	794	617	4110	675	139	3298	757	87	188	192
Atorvastatin	161	95	–	–	49	10	–	65	11	–	–	–
Bezafibrate	211	243	39	41	499	35	–	257	45	–	–	–
Carbamazepine	1399	1921	1767	1475	1085	1103	1128	1126	1038	1087	1031	979
Ciprofloxacin	202	176	21	23	23	22	15	16	11	–	–	–
Claritromicin	–	3402	521	448	3167	983	344	3687	775	463	236	208
Demetildiazepam	43	28	21	20	–	–	–	–	–	–	11	–
Enalapril	275	196	–	–	154	–	–	115	–	–	–	–
Deidro-Eritr. + Eritr.	–	1235	902	884	1334	640	410	543	297	390	306	241
Diclofenac	1713	1543	724	795	652	494	389	424	462	373	469	268
Estrone	84	70	8	13	54	77	–	47	85	–	11	–
Furosemide	1988	2160	230	802	1492	429	220	1687	469	220	569	605
Gemfibrozil	1719	1282	43	32	789	121	–	193	90	10	29	28
Ibuprofen	3770	3881	15	12	2959	33	–	2355	53	–	15	16
Idroclorotiazide	1269	1283	141	867	–	–	–	–	–	–	–	–
Ketoprofen	2123	2169	190	156	1718	352	53	1256	419	45	114	–
Naproxen	1806	2401	185	201	1880	62	30	1246	94	16	49	50
Ofloxacin	146	106	26	35	45	21	–	21	11	–	–	13
Ranitidine	1706	1617	202	192	1597	40	114	1288	42	75	130	133
Salbutamol	–	–	–	–	32	15	11	23	14	11	12	13
Sulfamethoxazole	511	339	52	129	383	24	121	320	24	100	74	75

Table C.9.: Ferrara WWTP influent (ng L^{-1})

Compounds	**Samples**			
	1st	**2**nd	**3**th	**4**th
Acetaminophen	498	839	763	1153
Atenolol	2100	1777	2080	2367
Atorvastatin	12	21	16	–
Azithromycin	330	20	92	–
Bezafibrate	115	71	63	111
Butalbital	72	251	101	110
Carbamazepine	300	488	1167	369
Chloramphenicol	22	16	13	24
Cimetidine	29	59	39	61
Ciprofloxacin	2100	1946	3700	1100
Clarithromycin	186	158	782	105
Clenbuterol	220	289	265	247
Codeine	86	92	100	150
Diazepam	–	16	–	–
Diclofenac	362	481	478	436
Enalapril	75	71	82	99
Enoxacin	81	108	130	90
Erithromycin	40	63	72	–
Famotidine	11	22	–	18
Fenofibrate	–	–	18	–
Fluoxetine	108	188	73	55
Furosemide	386	441	391	475
Gemfibrozil	281	169	156	197
Glibenclamide	96	81	85	88
Hydrochlorothiazide	1381	1673	5509	2323
Ibuprofen	959	928	1036	1181
Indomethacine	204	176	201	59
Ketoprofen	192	184	132	163
Loratadine	–	20	18	–
Lorazepam	214	239	173	249
Mefenamic acid	1024	557	1138	894

Metoprolol	220	289	265	247
Metronidazole	56	35	28	48
Mevastatin	161	275	133	122
Naproxen	828	906	782	814
Nifuroxazide	57	76	55	19
Norfloxacin	307	159	149	198
Ofloxacin	766	454	2222	574
Paroxetine	80	41	22	20
Pentobarbital	23	21	36	43
Phenobarbital	182	106	273	269
Phenylbutazone	129	130	98	67
Pindolol	–	–	11	–
Pravastatin	120	135	122	80
Propranolol	45	27	15	14
Propyphenazone	62	38	74	38
Ranitidine	116	93	128	108
Roxithromycin	139	49	62	–
Salbutamol	11	11	19	13
Salicylic acid	291	452	207	1044
Sotalol	369	614	517	637
Spiramycin	147	70	26	–
Sulfadiazine	13	25	26	24
Sulfamethazine	12	33	18	–
Sulfamethoxazole	385	278	735	375
Tilmicosin	218	304	460	21
Timolol	13	16	16	10
Trimethoprim	61	62	72	39
Average	**302**	**288**	**454**	**353**
Sum	**16298**	**16138**	**25443**	**16946**

Table C.10.: Ferrara WWTP effluent or CW influent (ng L^{-1})

Compounds	**Samples**			
	1st	**2**nd	**3**th	**4**th
Acetaminophen	58	23	27	12
Atenolol	711	976	703	546
Atorvastatin	–	–	14	–
Azithromycin	132	177	148	69
Bezafibrate	43	42	48	11
Butalbital	90	125	95	95
Carbamazepine	440	378	392	276
Cimetidine	29	49	32	12
Ciprofloxacin	623	516	1120	294
Clarithromycin	275	315	289	258
Clenbuterol	214	202	181	130
Codeine	70	82	61	52
Diclofenac	277	327	315	218
Enoxacin	97	31	65	50
Erithromycin	–	13	33	–
Fenofibrate	–	–	13	–
Fluoxetine	63	–	47	62
Furosemide	342	326	346	83
Gemfibrozil	111	175	106	42
Glibenclamide	54	74	77	14
Hydrochlorothiazide	971	1418	1222	1049
Ibuprofen	106	117	91	–
Indomethacine	129	60	85	118
Ketoprofen	94	106	84	56
Lorazepam	136	119	142	82
Mefenamic acid	906	396	664	688
Metoprolol	214	202	181	130
Metronidazole	27	41	29	13
Mevastatin	127	40	136	27
Naproxen	199	208	205	100
Nifuroxazide	23	–	12	–

Norfloxacin	159	165	149	137
Ofloxacin	359	523	479	215
Paroxetine	11	15	18	–
Pentobarbital	28	17	18	–
Phenobarbital	114	141	174	123
Phenylbutazone	59	37	60	51
Pravastatin	50	38	70	59
Propranolol	13	26	18	16
Propyphenazone	30	45	24	68
Ranitidine	74	104	90	44
Roxithromycin	17	34	53	13
Salbutamol	17	14	–	11
Salicylic acid	121	113	110	127
Sotalol	350	473	259	211
Spiramycin	22	50	31	19
Sulfadiazine	21	19	19	10
Sulfamethazine	15	11	11	–
Sulfamethoxazole	238	204	244	169
Tilmicosin	81	36	27	–
Timolol	–	12	–	–
Trimethoprim	37	51	36	37
Average	**174**	**180**	**177**	**138**
Sum	**8374**	**8664**	**8853**	**5796**

Table C.11.: Ferrara CW effluent (ng L^{-1})

Compounds	**Samples**			
	1st	**2**nd	**3**th	**4**th
Acetaminophen	21	18	–	–
Atenolol	386	573	369	204
Azithromycin	–	–	–	19
Bezafibrate	23	25	30	–
Butalbital	79	81	31	44
Carbamazepine	324	392	458	374
Cimetidine	21	38	23	11
Ciprofloxacin	292	147	302	91
Clarithromycin	266	311	299	185
Clenbuterol	159	180	179	129
Codeine	34	35	27	18
Diclofenac	284	278	332	190
Enoxacin	75	21	36	19
Fluoxetine	30	15	43	88
Furosemide	228	207	230	53
Gemfibrozil	110	128	76	24
Glibenclamide	42	52	53	22
Hydrochlorothiazide	634	309	520	267
Ibuprofen	53	48	74	–
Indomethacine	76	41	57	41
Ketoprofen	70	80	76	52
Lorazepam	104	114	132	72
Mefenamic acid	626	366	549	590
Metoprolol	159	180	179	129
Mevastatin	19	35	56	47
Naproxen	140	107	179	29
Norfloxacin	72	54	98	70
Ofloxacin	67	40	76	74
Pentobarbital	–	–	11	13
Phenobarbital	106	115	158	78
Phenylbutazone	13	22	24	34

Pravastatin	15	17	37	36
Propranolol	11	–	–	–
Propyphenazone	69	35	45	–
Ranitidine	67	53	50	14
Roxithromycin	13	15	83	57
Salicylic acid	107	107	108	117
Sotalol	320	452	273	178
Spiramycin	–	14	–	11
Sulfadiazine	13	23	26	18
Sulfamethoxazole	148	153	248	170
Trimethoprim	27	26	32	14
Average	**136**	**123**	**144**	**97**
Sum	**5304**	**4925**	**5607**	**3581**

Table C.12.: Sulfamethoxazole, Ciprofloxacin, Trimethoprim concentration (μg L^{-1}) in Ferrara CW during the final experimental campaign

Date	**Sul**		**Cipro**		**Trim**	
	In	**Out**	**In**	**Out**	**In**	**Out**
30 March 2010	43	62	3.55	0.52		
01 April 2010	59	65	1.96	0.42		
02 April 2010	283	65	4.02	0.54		
06 April 2010	45	98	2.04	0.34		
07 June 2010	48	64	1.57	0.3		
08 June 2010	355	44	1.26	0.32		
19 May 2010	29	33	4.09	0.17	8	3
20 May 2010	31	10	0.97	0.11	7	3
21 May 2010	14	18	0.49	0.18	4	2
22 May 2010	24	14	0.44	0.1	12	3
26 June 2010	26	16	0.47	0.11	20	6
27 June 2010	36	104	0.26	0.07	16	6
Average	**83**	**49**	**1.76**	**0.27**	**11**	**4**
Sum	**993**	**593**	**21.12**	**3.18**	**67**	**23**

APPENDIX D

Publications

This appendix reports all the scientific publications made in these research years. Not all the work done in these years were about PhCs because other research activities were open in the Sanitary and Environmental Engineering group at the Department of Engineering of Ferrara.

In particular some paper were about the concept of water reuse using natural treatment and other paper treated specifically concept like PhCs and hospital, the real aim of this thesis.

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A promising practice to reclaim treated wastewater for reuse: Chemical disinfection followed by natural systems

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Abstract

The availability of freshwater to meet different water needs has raised serious concerns in the last decades all around the world. Water scarcity, deterioration of quality and increasing demand have led to the development and use of alternative sources of water. Reclamation and recycling are now considered as key components of water and wastewater management policies around the world. In this context, the adoption of *soft* wastewater treatments with a minimum use of chemical agents and having minimum environmental impact is widely encouraged.

An experimental campaign was carried out on a pilot plant which consisted of a two-stage disinfection system for a secondary biological effluent. Disinfection consisting of a chemical step (mild chlorination) followed by a natural one (filtration through a horizontal subsurface flow (HSF) bed) was tested in order to evaluate the possibility of producing a final effluent adequate for agricultural reuse.

The investigation has shown that this combined system, with low doses of NaClO (2 mg L^{-1} of disinfectant and a retention time of 30 min, corresponding to an applied dose of $2 \times 30 = 60$ mg L^{-1} min^{-1}) and a well designed final subsurface flow system (at least 1 m^2 EI^{-1}) is able to obtain an effluent complying with reuse quality limits, in particular for microbiological parameters.

For HSF design parameters, neither filling material, aspect ratio nor vegetation type (*Phragmites australis* and turf) caused significant differences in the average levels of COD, suspended solids, NH_4, total phosphorus and *Escherichia coli* concentrations in the effluent.

Finally in order to protect HSF bed from substrate clogging and to prolong its working life, a rapid sand filter was placed before the bed and its impact analyzed. It was demonstrated that the filter was able to retain occasional but unavoidable activated sludge carry-overs from the secondary clarifier which otherwise would rapidly accumulate in the front region of the bed resulting in poor performance (overflows and medium clogging) in quite short time.

Keywords: Disinfection; Experimental investigation; Polishing chemical and natural treatment; Reuse; Clogging prevention

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Figure D.1.: Verlicchi, P., Galletti, A., Masotti, L.: *A promising practice to reclaim treated wastewater for reuse: Chemical disinfection followed by natural systems.* Desalination 247 (2009), 490-508

Management of hospital wastewaters: the case of the effluent of a large hospital situated in a small town

Paola Verlicchi, Alessio Galletti and Luigi Masotti

ABSTRACT

Hospitals are the main source of pharmaceutical compounds (PhCs) released into the environment. Generally, their discharges are co-treated with domestic wastewaters, resulting in a decrement of the recalcitrant compound concentrations in the final effluent due to water dilution. However, as many PhCs resist normal treatments, pollutant load does not change. This paper compares the chemical characteristics of hospital and domestic wastewaters on the basis of an experimental investigation for macro-pollutants and literature data for PhCs. A membrane biological reactor pilot plant fed by a hospital effluent is tested in order to evaluate the feasibility of treating these kinds of wastewaters with membrane systems. The paper then presents the possible scenarios in the management of the effluent of a large hospital situated in a small town. In particular, it reports on a case study of designing a (new) treatment plant for the effluent of the 900 bed hospital in Ferrara, Northern Italy, located on the outskirts of the town. Finally, costs for the intervention are given.

Key words | best technologies, costs analysis, domestic wastewaters, experimental investigation, hospital wastewater, pharmaceutical compounds

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INTRODUCTION

Hospital wastewaters (HWws) are composed of the effluents of three different services: (i) general services (kitchen, internal laundry, heating and cooling systems), (ii) diagnostic services (laboratories, radiology departments, outpatient departments, transfusion centres) and (iii) wards (general medicine, surgery, specialities, haemodialysis, etc.). In Italy and in many other countries, by law, the effluents from specific wards or services (such as nuclear medicine or histological laboratories) that contain radioactive wastes or anatomical parts cannot be discharged into the hospital sewage network, but must be collected in adequate hermetic baskets and given to authorized disposal firms (Emilia Romagna Region Guidelines 2009).

By law, HWws are often considered to be of the same pollutant nature as domestic wastewaters (DWws), and so they are generally discharged into (municipal) sewer networks, collected at a wastewater treatment plant (WWTP) and treated along with DWws. The only pre-treatment that could be required before entering the sewer is a mild chlorination of the whole effluent in order to reduce its microbiological load.

WWTPs were originally built, and have more recently been upgraded, with the aim of removing carbon, nitrogen and phosphorus compounds in addition to the microbiological organisms which are the pollutants regularly arriving at the plant in concentrations to the order of mg/L and at least 10^5 CFU/100 ml. HWws represent a unique kind of wastewater due to the nature and quantity of the micropollutants which are typically present at μg/L: active substances of medicines and their metabolites, chemicals, heavy metals, disinfectants and sterilizers, radioactive markers, (Emmanuel *et al.* 2001; Kummerer 2001; Altin *et al.* 2003; Jones *et al.* 2005). Moreover, HWw flow rates generally amount to only a small percentage of the

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Figure D.2.: Verlicchi, P., Galletti, A., Masotti, L., *Management of Hospital Wastewaters. The case study of the Effluent of a Large Hospital Situated in a Small Town*, Water Science and Technology, 61.10 (2010), 2507-2519

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Review Paper

Hospital effluents as a source of emerging pollutants: An overview of micropollutants and sustainable treatment options

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SUMMARY

Hospital wastewaters contain a variety of toxic or persistent substances such as pharmaceuticals, radionuclides, solvents and disinfectants for medical purposes in a wide range of concentrations due to laboratory and research activities or medicine excretion. Most of these compounds belong to the so called *emerging contaminants*; quite often unregulated pollutants which may be candidates for future regulation depending on research on their potential health effects and monitoring of their occurrence. Their main characteristic is that they do not need to persist in the environment to cause negative effects since their high transformation/removal rates can be compensated for by their continuous introduction into the environment.

Some of these compounds, most of them pharmaceuticals and personal care products may also be present in urban wastewaters. Their concentrations in the effluents may vary from ng L^{-1} to μg L^{-1}.

In this paper, hospital effluents and urban wastewaters are compared in terms of quali–quantitative characteristics. On the basis of an in-depth survey: (i) hospital average specific daily water consumptions (L patient^{-1} day^{-1}) are evaluated and compared to urban ones (L person^{-1} day^{-1}), (ii) conventional parameters concentrations in hospital effluents are compared to urban ones and (iii) main pharmaceuticals and other emerging compounds contents are compared in the two wastewaters. Finally, an overview of the removal capacity of the different treatments is reported.

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Contents

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Figure D.3.: Verlicchi, P., Galletti, A., Petrovic, M., Barceló, D., *Hospital effluents as a source of emerging pollutants: an overview of micropollutants and sustainable treatment options.* Journal of Hydrology, 389 (2010), 416-428

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Removal and accumulation of Cu, Ni and Zn in horizontal subsurface flow constructed wetlands: Contribution of vegetation and filling medium

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ABSTRACT

This study investigated the accumulation and removal of Cu, Ni and Zn in two horizontal subsurface flow constructed wetlands for domestic wastewater treatment, which differ by shape, presence of macrophytes and water depth. Between March and December 2007, the three metals were measured in the influent and effluents of the two systems. Average percentage removal rates were extremely low for Cu (3% and 9% in the two beds) and higher for Zn and Ni (between 25 and 35%). Under higher Zn influent concentrations, it was found to be between 78–87%, which is in agreement with other literature data.

During the peak standing crop season (August), biomasses of the different parts of *Phragmites australis* (stems, leaves and flowers, roots and rhizomes) were analysed in terms of weight and heavy metal concentration in order to assess heavy metal distribution among the tissues. It was found that the plants contribute to total heavy metal removal to a lesser extent than the filling medium. Aboveground tissues remove 34% of Cu, 1.8% of Ni and 6.2% of Zn % and, once harvested, their disposal does not appear to pose a problem for the environment. If heavy metals are present at high concentrations in the horizontal subsurface flow bed influent, over time, their accumulation in the filling medium could necessitate special care in the bed's management to avoid release into the surrounding environment.

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1. Introduction

Constructed wetlands with a horizontal subsurface flow (H-SSF) are commonly used for domestic wastewater treatment, but there are further applications for other types of wastewaters such as effluents from food processing, abattoirs, pulp and paper production, and textile industries as well as municipal solid wastes (MSW) landfill leachate. In general, H-SSF systems are extensively monitored for macropollutants, including BOD_5, COD, suspended solids, nitrogen and phosphorus compounds and bacteria (Kadlec and Knights, 1996; Vymazal et al., 1998; Sundaravadivel and Vigneswaran, 2001).

Fewer studies have looked at trace elements in H-SSF systems, although lately there has been a growing interest in evaluating such systems ability and reliability in removing micropollutants, particularly heavy metals (HMs), from domestic and industrial wastewaters (Scholz and Xu, 2002; Vymazal and Krasa, 2003; Ranieri, 2004), MSW landfill leachate (Peverly et al., 1995; Yalcuk and Ugurlu, 2009), and acid mine drainage (Mays and Edwards, 2001; Deng et al., 2004).

In recent years, some studies have investigated the behaviour of plants in the presence of HMs. Among them, Miretzky et al. (2004) and Hassan et al. (2007) examined the removal rates of some elements, Drost et al. (2007) investigated the toxicity of HMs on plants, Dunbabin and Bowmer (1992) analysed the use of these plants as biofilters for polluted waters, Cardwell et al. (2002) evaluated biomonitoring of metals, Deng et al. (2004) and Mishra et al. (2008) investigated HMs uptake by duckweed (*Lemna minor*), water hyacinth (*Eichoria crassipes*), Salix, cattail (*Typha latifolia*) and common reed (*Phragmites australis*).

The HM concentration ranges vary depending on the origin of the wastewaters. Table 1 shows the observed ranges of HMs concentrations in raw domestic and industrial wastewaters (mainly refinery, chemical and plastic factories), in different types of surface runoff (parking areas, roofs, roads), MSW landfill leachate, and acid mine drainage.

The main difficulty in treating wastewaters containing HMs is due to the fact that they cannot be *destroyed* or *degraded*. HMs can accumulate in binding sites within the filling medium or precipitate during their passage through the plant.

H-SSF beds are dynamic micro-systems in which many physical, chemical and biological mechanisms may occur simultaneously. These mechanisms are strictly correlated to filling medium conditions (*i.e.*: structure, chemical composition, biofilm and sediments characteristics), environmental conditions (mainly aerobic/anaerobic/anoxic conditions, temperature and pH), and operational conditions (mainly water chemical characteristics and flow rate) which may change over time.

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Figure D.4.: Galletti A., Verlicchi P., Ranieri E., *Removal and accumulation of Cu, Ni and Zn in horizontal subsurface flow constructed wetlands: contribution of vegetation and filling medium*. Science of the Total Environment, 408 (2010) 5097-5105

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Wastewater polishing index: a tool for a rapid quality assessment of reclaimed wastewater

Paola Verlicchi · Luigi Masotti · Alessio Galletti

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Abstract A new index, the *Wastewater Polishing Index* (WWPI), has been defined for the rapid assessment of the quality achieved by different polishing treatments for water discharged into surface water bodies and for reuse purposes. The index is defined by a weighted average of six parameters (SS, BOD_5 COD, ammonia, total phosphorus, and *E. scherichia coli*), each transformed onto a sub-index scaled from 0 to 100. *E. coli* has been assigned a greater weight than the other indicators. The index is equal to 0 if none of the six pollutants are present in the effluent and to 100 when all six parameters equal their corresponding Italian legal limits for discharge into surface water bodies. When all six of them equal their corresponding Italian legal limits for reuse, the WWPI is 36. The index has been validated and tested on a pilot plant including a rapid sand filtration, a slow filtration through a horizontal subsurface flow system and a lagooning, in addition to their combinations. The experimental investigation showed that the index is a good tool for (1) rapidly comparing the water quality achieved by different treatment sequences, particularly natural systems; (2) rapidly evaluating whether the proposed sequence is able to produce an effluent adequate for reuse; and (3) rapidly evaluating the water quality improvement achieved by different systems. The proposed index could be of great help for managers and decision makers when planning for water resources, in particular, for comparing the quality level achieved by different wastewater treatment sequences.

Keywords Experimental validation · Natural treatments · Polishing treatments · Reuse · Sensitivity analysis · Water quality index

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Introduction

A water quality index is a unitless number that ascribes a quality value to an aggregate set of measured chemical, physical, and microbiological parameters. Generally, water quality indices consist of sub-index scores assigned to each parameter by comparing its measurement with a parameter-specific rating curve, optionally weighted and

Figure D.5.: Verlicchi P., Masotti L., Galletti A., *Wastewater Polishing Index: a tool for a rapid quality assessment of reclaimed wastewater*, Environmental, Monitoring and assessment, 173 (2011) 267-277

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Subject
Dichiarazione di conformità della tesi di dottorato
Io sottoscritto Dott. (Cognome e Nome)
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Composti farmaceutici nelle acque. Indagine sugli effluenti ospedalieri come fonte di contaminazione ambientale e sulla loro trattabilità
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Pharmaceutical compounds in waters. Investigations on hospital effluents as a source of environmental contamination and on their treatability
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CONSAPEVOLE --- 1) del fatto che in caso di dichiarazioni mendaci, oltre alle sanzioni previste dal codice penale e dalle Leggi speciali per l'ipotesi di falsità in atti ed uso di atti falsi, decade fin dall'inizio e senza necessità di alcuna formalità dai benefici conseguenti al provvedimento emanato sulla base di tali dichiarazioni; -- 2) dell'obbligo per l'Università di provvedere al deposito di legge delle tesi di dottorato al fine di assicurarne la conservazione e la consultabilità da parte di terzi; -- 3) della procedura adottata dall'Università di Ferrara ove si richiede che la tesi sia consegnata dal dottorando in 4 copie di cui una in formato cartaceo e tre in formato .pdf, non modificabile su idonei supporti (CD-ROM, DVD) secondo le istruzioni pubblicate sul sito : http://www.unife.it /dottorati/dottorati.htm alla voce ESAME FINALE – disposizioni e modulistica; -- 4) del fatto che l'Università sulla base dei dati forniti, archivierà e renderà consultabile in rete il testo completo della tesi di dottorato di cui alla presente dichiarazione attraverso l'Archivio istituzionale ad accesso aperto "EPRINTS.unife.it" oltre che attraverso i Cataloghi delle Biblioteche Nazionali

Centrali di Roma e Firenze. --- DICHIARO SOTTO LA MIA RESPONSABILITA' --- 1) che la copia della tesi depositata presso l'Università di Ferrara in formato cartaceo, è del tutto identica a quelle presentate in formato elettronico (CD-ROM, DVD), a quelle da inviare ai Commissari di esame finale e alla copia che produrrò in seduta d'esame finale. Di conseguenza va esclusa qualsiasi responsabilità dell'Ateneo stesso per quanto riguarda eventuali errori, imprecisioni o omissioni nei contenuti della tesi; -- 2) di prendere atto che la tesi in formato cartaceo è l'unica alla quale farà riferimento l'Università per rilasciare, a mia richiesta, la dichiarazione di conformità di eventuali copie; -- 3) che il contenuto e l'organizzazione della tesi è opera originale da me realizzata e non compromette in alcun modo i diritti di terzi, ivi compresi quelli relativi alla sicurezza dei dati personali; che pertanto l'Università è in ogni caso esente da responsabilità di qualsivoglia natura civile, amministrativa o penale e sarà da me tenuta indenne da qualsiasi richiesta o rivendicazione da parte di terzi; -- 4) che la tesi di dottorato non è il risultato di attività rientranti nella normativa sulla proprietà industriale, non è stata prodotta nell'ambito di progetti finanziati da soggetti pubblici o privati con vincoli alla divulgazione dei risultati, non è oggetto di eventuali registrazioni di tipo brevettale o di tutela. --- PER ACCETAZIONE DI QUANTO SOPRA RIPORTATO

Firma Dottorando

Ferrara, lì _20 gennaio 2011_____ Firma del Dottorando

_____ Alessio Gilletti _____

Firma Tutore

Visto: Il Tutore Si approva Firma del Tutore _____ Paola Verlicchi _