UNIVERSITY OF CALIFORNIA

Los Angeles

Removal of Emerging Contaminants in Biological Treatment

A thesis submitted in partial satisfaction

of the requirements for the degree Master of Science

in Civil Engineering

by

Sheng-Chieh Wang

2009

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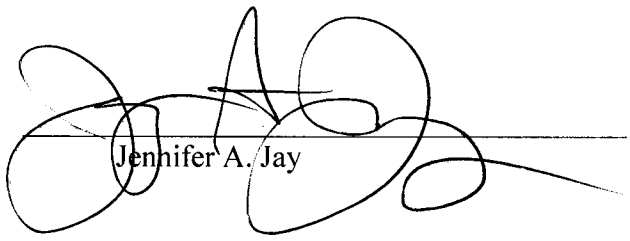

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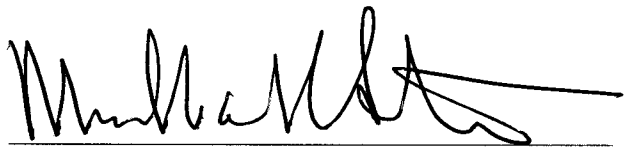

Michael K. Stenstrom, Committee Chair

University of California, Los Angeles

2009

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ABSTRACT OF THE THESIS

Removal of Emerging Contaminants in Biological Treatment

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Master of Science in Civil Engineering

University of California, Los Angeles, 2009

Professor Michael K. Stenstrom, Chair

Emerging contaminants as endocrine disrupting compounds (EDCs) or pharmaceuticals and personal care products (PPCPs) are of increased interest in water pollution control in recent years. The majority of EDCs and PPCPs are more polar than traditional contaminants and several have acidic or basic functional groups. These properties and occurrences at trace level form unique challenges for both removal process and analytical detection of these contaminants. In this thesis, several selected EDCs and PPCPs with high occurrence frequency are discussed to understand the relevance between their chemical properties and removal efficiency. Three removal mechanisms are involved in

biological treatment process, which are sorption, volatilization, and biological degradation. Sorption and biodegradation are the main mechanisms to removal EDCs and PPCPs while volatilization has negligible removal for pharmaceuticals. The sorption efficient (K_d), octanol-water partition coefficient (K_{ow}), and pseudo first-order constant (k_{biol}) can influence the removal performance of emerging contaminants. Compounds with high kbiol and low K_d can be totally removed through biological degradation. Compounds with low K_{ow} have less interaction with sludge, which they are unable to be removed through sorption. The solid retention time (SRT) is an important parameter for both sorption and biodegradation. Generally speaking, biological degradation of PPCPs can be enhanced by increasing the SRT. Membrane bioreactors (MBRs) have similar performance on the removal of emerging contaminants. The explanation of why MBRs can reach high removal rate is the operation under long SRT. Future research needs include more detailed fate and transport data, standardized analytical methodology, predictive models, removal kinetics, and determination of the toxicological relevance of trace levels of EDCs and PPCPs in water.

Key words: endocrine disrupting compounds; pharmaceutical; sorption; biological degradation; solid retention time

1. Introduction

The issue of emerging contaminants and their metabolites in the aquatic environment has raised increasing concern in recent years. New compounds are continuously being manufactured and released to the environment in various ways. These so-called “emerging” or “new” contaminants are still unregulated and have become an environmental problem and public health issue. It is strongly recommended that this kind of contamination require legislative intervention depending on research on their potential health effects and monitoring data regarding their persistence in the environment. Emerging contaminants mainly comprise products used in everyday life in large quantities, such as endocrine disrupting compounds (EDCs), pharmaceutical and personal care products (PPCPs), surfactants and surfactants residues, and various industrial additives.

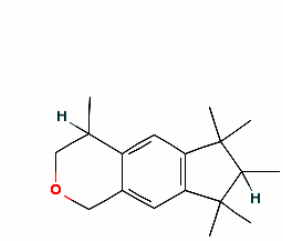
1.1 Endocrine disrupters (EDCs)

Endocrine disrupters (also called hormonally active agents) are any type of chemical or mixture of chemicals that affect the endocrine system, and cause negative reproductive and developmental health effects for the human or animal and/or their offspring. The endocrine system is a complex network of organs, including the thyroid, pancreas, pituitary, ovaries, testes, and adrenal glands, which secrete hormones into the bloodstream to target cell receptors in other organs or tissues, where the hormone has a specific effect. (Pontius 2001; Symons et al. 2000) The Environmental Protection Agency (EPA) has defined environmental endocrine disrupting compounds (EDCs) as exogenous agents that interfere with the “synthesis, secretion, transport, binding, action or elimination of nature hormones in the body that

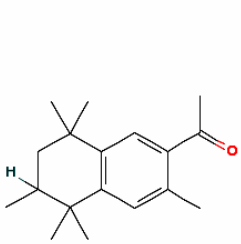
are responsible for the maintenance of homeostasis, reproduction, development, and/or behavior." However, definitions and opinions that define an EDC vary greatly. In general, there are three major classes of endocrine disrupting compounds, which are estrogenic (compounds that mimic or block natural testosterone), androgenic (compounds that mimic or block natural testosterone), and thyroidal (compounds with direct or indirect impacts to the thyroid).

1.2 Pharmaceutical and personal care products (PPCPs)

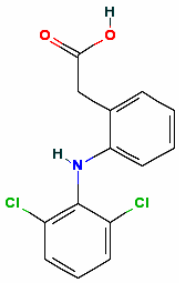
Pharmaceutical and personal care products (PPCPs)are largely consumed in modern societies and constitute a wide number of compounds, including drugs (antibiotics, tranquillizers, anti-epileptics, etc.), hormones (natural and synthetic), X-ray contrast media, musk fragrances, etc., which, until recently, have not been of major concern with regard to their environmental effects. When these substances are freely discharged into the environment, they could cause some impact on aquatic and terrestrial organisms (Fent et al. 2006; Jjemba 2006), since they have been specifically designed to produce biological effects even at very low concentrations. In addition, some of PPCPs bioaccumulate. Bioaccumulation refers to the tendency to increase in concentration when a toxin is consumed in a successional food chain. Two main pathways can be distinguished during metabolism: (1) phase I, where hydrolysis, oxidation, reduction, alkylation and dealkylation reactions occur, and (ii) phase II, where conjugates, mainly glucuronides and sulfonates, are formed in order to enhance excretion (Cunningham 2004). Table 1 shows the most common PPCPs and their application.



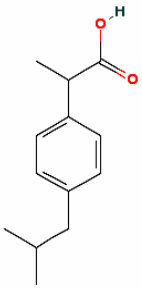
Galaxolide (HHCB)



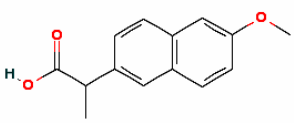
Tonalide (AHTN)



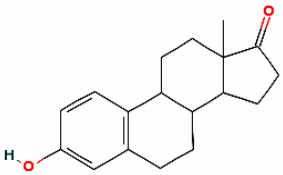
Diclofenac (DCF)



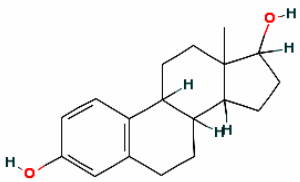
Ibuprofen (IBP)



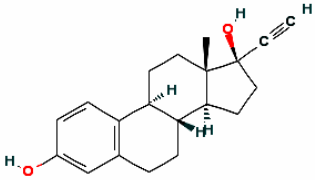
Naproxen (NPX)



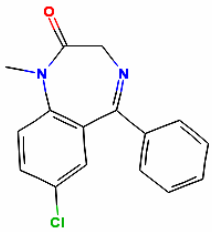
Estrone (E1)



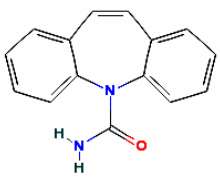
17β-estradiol (E2)



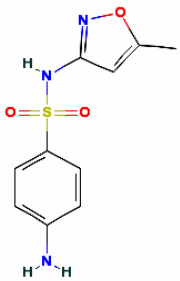
17α-ethinylestradiol (EE2)



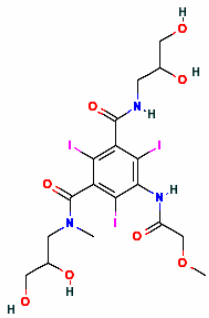
Diazepam (DZP)



Carbamazepine (CBZ)



Sulfamethoxazole (SMX)



Iopromide (IPM)

Figure 1. Chemical Structure of selected PPCPs (http://pubchem.ncbi.nlm.nih.gov)

Table 1. Principal emerging PPCPs compounds and their application

Application	Compound
Pharmaceuticals	
Veterinary & human antibiotics	Trimethoprim, erytromycine, lincomycin, sulfamethaxole, chloramphenicol, amoxycillin
Analgesics & anti-unflammatory drugs	Ibuprofen, diclofenac, fenoprofen, acetaminaohen, naproxen, acetylsalicylic acid, fluoxetine, ketoprofen, indometacine, paracetamol
Psycguatruc drugs	Diazepam, carbamazepine, primidone, salbutamol
Lipid regulators	Clofibric acid, bezafibrate, fenofibric acid, etofibrate, gemfibrozil
β-Blockers	Metoprolol, propranolol, timolol, sotalol, atenolol
X-ray contrasts	Iopromide, iopromide, iopamidol, diatrizoate
Steroids & hormones	Estradiol, estrone, estriol, diethylstilbestrol (DES)
Personal care products	
Fragrances	Ntiro, polycyclic and macrocylic musks; phthalates
Sun-screen agents	Benzophenone, methylbenzylidene camphor
Insect repellents	N,N-diethyltoluamide
Antiseptics	Triclosan, chlorophene

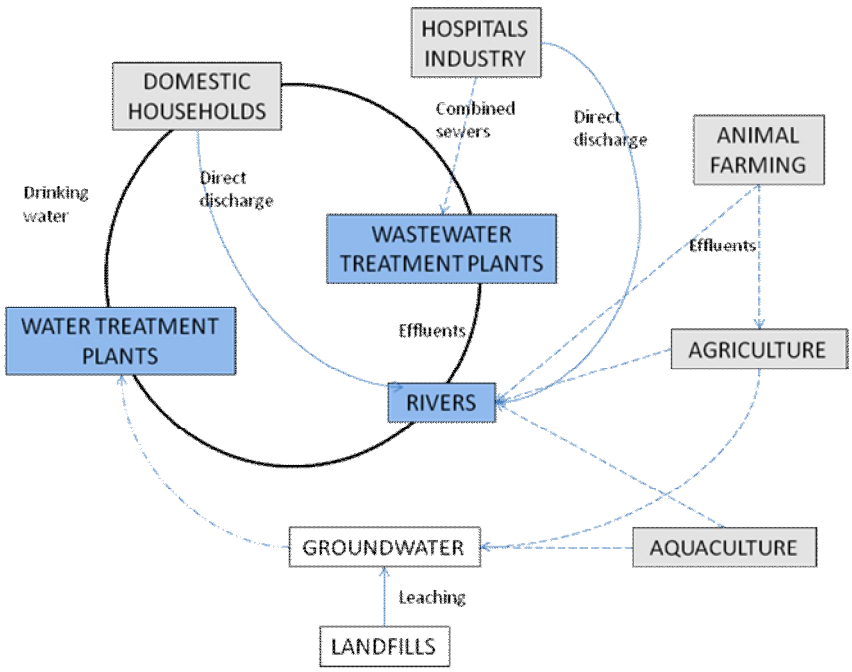


Figure 2. Pathways of emerging contaminants (Petrovic et al. 2003)

1.3 Pathways of PPCPs

Discharge of PPCPs can occur from domestic wastewater, hospital wastewaters or industrial discharges. PPCPs eventually enter wastewater treatment plants (WTPs). During wastewater treatment, a distribution occurs between the dissolved and solid phases. Influent suspended solids are largely removed through primary clarification. The separation is relevant for the most lipophilic compounds. As a result, non-degraded PPCPs will be discharged into the environment not only through the final effluent of the plant, but also with biosolids.

Kinney et al. (2006) showed that organic wastewater contaminants could be detected in the target biosolids with high occur frequency and high concentration, which suggests that biosolids can be an important source of organic wastewater contaminants to terrestrial environment. Xia et al. (2005) indicated that the PPCPs that enter wastewater treatment plants can undergo partial or complete transformation and by-products can be discharged to the environment in the final effluent or through biosolids being applied to land.

One of the main sources of emerging contaminants is untreated urban wastewater and effluents from wastewater treatment plants. Most current wastewater treatment plants are not designed to treat these compounds. As a result, a high portion of emerging contaminants and their metabolites can pass through the treatment process and enter the aquatic environment via wastewater effluents without any elimination. (Figure 2)

1.4 Toxicity of emerging contaminants to the environment

The effect and hazard of emerging contaminants to public health and environment

are poorly understood. Pharmaceuticals are a class of emerging environmental contaminants that are extensively and increasingly being used in human and veterinary medicine. These chemicals are designed to have a specific mode of action, and they have varying persistence in the body. These features among others suggest that it is important to evaluate the effect of pharmaceuticals on aquatic flora and fauna.

Ecotoxicity of emerging contaminants can be divided in to two aspects: acute and chronic. The present research indicates that LC50 or EC50 concentrations for PPCP such as fluoxetine and diazepam are approximately 100 times greater than commonly observed environmental concentrations. There is a general lack of chronic toxicity data on pharmaceuticals, in particular in fish. Many pharmaceuticals need more investigation to determine potential long-term ecotoxicological effects, particularly with respect to potential disturbances in hormonal homeostasis (endocrine disruption), immunological status, or gene activation and silencing during long-term exposure (Fent et al. 2006).

Drugs may also induce unexpected effects in nonmammalian organisms based on the differences in their pharmacokinetics and pharmacodynamics, important parameters for occurring species differences. Disturbances of the reproductive system and hormone system, immune depression, neurobehavioral changes, to name some key targets, may have far reaching effects on the population level. This has become evident for endocrine disrupters such as steroid hormones used in contraceptives resulting in important adverse effects at environmentally relevant concentrations (Jobling et al. 1998; L¨ange et al. 2001; Thorpe et al. 2003; Parrott and Blunt 2005).

Another problem stemming from emerging contaminants is antibiotic-resistant

bacteria. When drugs are excreted in waste, the compounds linger in the environment. In the case of livestock waste, the antibiotic-laced manure is spread directly onto farm crops as fertilizer. From there it may run off into nearby streams. The result is that bacteria are able to mutate into strains that are resistant to the widely spread antibiotics, creating infections that cannot be easily cured. According to the Centers for Disease Control and Prevention, about 2 million people in hospitals get infections each year, which cause 90,000 deaths. Of these, more than 70 percent of the bacteria that causes these infections are resistant to at least one common antibiotic that is typically used to treat them. Table 2 shows several of the most frequently detected EDCs and PPCPs in the environment.

1.5 U.S. regulation issues

Several compounds now known to be endocrine disruptors, including arsenic, cadmium, and some phenols were included in Public Health Services Standard. The principal law to govern drinking water safety is the Safe Drinking Water Act in 1974. This law required the US EPA to establish a standard to rule the maximum levels of various contaminants including some compounds with endocrine disruption characteristics in drinking water. However, not until 1995 with amendments to the Safe Drinking Water Act (bill number S.1316) and Food Quality Protection Act (bill number P.L. 104-170) was endocrine disruption be specifically defined in any United States legislation. These two laws regulated that chemical and formulations should be tested for potential endocrine activity before they are manufactured or used in certain

Table 2. Compounds with highest frequency of detection in recent USGS EDC/PPCP survey of U.S. streams (Kolpin et al., 2002)

Compounds	Use	Frequency of detection (%)
Coprostanol	Estrogen	~80%
Cholesterol	Plant/animal steroid	~80%
N-N-diethyltoluamide	Mosquito repellant	~80%
Caffeine	Stimulant	~75%
Tris(2-chloroethyl)phosphate	Fire retardant	~75%
Triclosan	Antibiotic	~60%
4-Nonylphenol	Surfactant	~60%
4-Nonylphenol monoethoxylate	Surfactant	~50%
Ethanol, 2-butoxy-phosphate	Plasticizer	~45%
4-Octylphenol monoethoxylate	Surfactant	~45%
Bisphenol A	Plasticizer	~45%
Cotinine	Nicotine metabolite	~35%
4-Nonylphenol diethoxylate	Surfactant	~35%
5-Methyl-1H-benotrizole	Antioxidant	~30%
Fluoranthene	PAH	~30%
1,7-Dimethylxanthine	Caffeine metabolite	~30%
Pyrene	PAH	~25%
Trimethoprim	Antibiotic	~25%
1,4-Dichlorobenzene	Deodorizer	~25%
Acetaminophen	Analgesic	~25%
Tetrachloroethylene	Solvent	~20%
4-Octylphenol diethoxylate	Surfactant	~20%
Erythromycin-H2O	Antibiotic	~20%
Estriol	Estrogen	~20%
Lincomycin	Antibiotic	~15%
Sulfamethoxazole	Antibiotic	~15%
Phthalic anhydride	Plasticizer	~15%
Carbaryl	Insecticide	~15%

process where drinking water and/or food could become contaminated. According to these laws, the EPA is required to "develop a screening program, using appropriate validated test systems and other scientifically relevant information, to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effect as the Administrator may designate."

In order to develop the system, the EDSTAC was formed by the EPA to provide recommendations on a conceptual framework, priority setting, screening, and testing methodologies, and communication and outreach programs. A final report was made in July of 1998 which recommended that that human and wildlife impacts be considered, and that estrogen, androgen, and thyroid (EAT) end points be examined (EPA, 1998). Furthermore, EDSTAC also recommended the evaluation of mixtures of chemicals in breast milk, baby formulas, hazardous waste sites, pesticides and fertilizers, drinking water DBPs, and gasoline. The Endocrine Disruptor Methods Validation Subcommittee (EDMVS) was formed in 2001 to evaluate the test series suggested by EDSTAC. The tasks of EDSTAC is to evaluate the methods by determining (1) ability to be transferred to other laboratories, (2) sensitivity to EAT end point, (3) proper standard operation process, and (4) validation with representative chemicals. The outcome of this screening battery is critical to the water industry, as it designed to definitively identify EDCs. However, since the current legislation only regulates the raw chemicals produced or used in the industries, these action may have rare immediate effect on water and wastewater treatment regulations.

Currently, there is no federal regulation for pharmaceuticals in drinking or natural waters. The Food and Drug Administration (FDA) requires ecological testing

and evaluation of a pharmaceutical only if an environmental concentration in water or soil is expected to exceed 1 mg/L or 100 mg/kg, respectively (FDA, 1998). Concerning the recent observations on the occurrence and concentration of PPCPs in the aquatic environment, the government should reconsider this policy. Toxicological studies conducted at environmentally relevant concentrations are necessary for intelligible regulations to be established.

2. Analysis Method of emerging contaminants

Since EDCs represent a wide variety of compounds, it is important to define which EDCs one seeks to analyze. DDT and other organochlorine pesticides can be defined as EDCs. Several classes of EDCs and PPCPs contain polar functional groups. As a result, the major novel analytical work is focused on trace levels of less characterized contaminants with greater polarity than many of the "classic" contaminants. There is no standard method currently available for emerging contaminants. Moreover, since a few commercial laboratories analyze these compounds, the data of characterizing EDCs and PPCPs is rare.

There are various analytical methodologies which have been applied for the quantification of EDCs and PPCPs in water. Yoon et al. (2003) did a direct measurement by using high-performance liquid chromatography (HPLC) to measure the adsorption of three estrogenic compounds (bisphenol A (BPA), 17β-estradiol (E2), and 17α-ethynyl estradiol (EE2)) on several powdered activated carbons (PAC). However, the major methods used to measure emerging contaminants involve an extraction procedure followed by instrumental analyses.

Several analytical methods for PPCPs have already been published in the

literature. Many of them are based on liquid chromatography–tandem mass spectrometry (LC–MS/MS) (Miao et al. 2002; Lee et al. 2007; Gomez et al. 2006). However, interference or important signal suppression caused by sample extracts continues to be a major issue, especially with untreated or poorly treated wastewater samples. Matrix effects are frequently observed when the LC–MS/MS electrospray ionization mode is used (Gomez et al. 2006). Furthermore, the cost of operating a LC–MS/MS system is an important consideration for many research or monitoring laboratories.

Gas chromatography–mass spectrometry (GC–MS) instrumentation is another steady method for analyzing PPCPs. However, this method requires the derivatization of carboxylic acid and hydroxyl moieties to some less polar groups. Several methodologies for determination EDCs and PPCPs in water used solid-phase extraction (SPE) followed by GC–MS.

Yu et al. (2007) optimized the analytical method based on solid-phase extraction (SPE) followed by gas chromatography–mass spectrometry (GC–MS) to derivate the target analytes in the eluted extract from surface and tap water. The method was developed successfully for most of the selected compounds [i.e. ibuprofen, salicylic acid, gemfibrozil, naproxen, triclosan, propranolol, diclofenac, carbamazepine, 4-octylphenol (OP), 4-nonylphenol (NP), nonylphenol-monoethoxylate (NP1EO), nonylphenoxyacetic acid (NP1EC), estrone (E1), and 17α-ethinyloestradiol (EE2)]. The recovery rate ranged from 47 – 109%. Typical limits of detection were less than 5 ng/L in tap water and less than 10 ng/L in river water. Lajeunesse et al. (2007) used SPE and gas chromatography–tandem mass spectrometry (GC–MS/MS), and indicated that the quantification limits of the analytical procedure ranged from 30 to

60 ng/L for 500mL of municipal wastewater. he best recovery rates ranged from 72 to 102%. Rice et al. (2007) indicated that by using microwave-assisted solvent extraction (MASE) followed by GC-MS, among seven target PPCPs, testing of the method on spiked soil allowed for 89.6±2.89% recovery of three target compounds and 25.0±1.93% recovery of five of the compounds. Detection limit ranged from 5 to 25 ng L^{-1}.

The understanding of the removal of EDCs and PPCPs in water treatment system is limited because of the lack of analyses for these compounds. Moreover, when these substances are detected, most of the concentrations they show are near analytical method detection limits. Most of the studies researching the removal of EDCs and PPCPs in wastewater treatment are conveyed from laboratory or bench-scale experiments. When the data on removal of EDCs and PPCPs are not available, making prediction based on results of previous researches using contaminants exhibiting similar characteristics may be possible.

3. Removal mechanism

3.1 Volatilization

Volatilization was an important removal mechanism for the low-molecular weight compounds in the spreading basins; between 30 and 70% of the chlorinated benzenes and 1- and 2- carbon halogenated organic compounds were removed in this way (Yu et al. 2006).

The process converts a chemical substance from a liquid or solid state to a gaseous or vapor state. The fraction of compound volatilized in the aeration tank (/) depends on the flow of air getting in contact with wastewater (Q_{air}), type of aeration

and Henry coefficient (H), as shown in Eq. 1 (Suarez et al. 2008).

$$\phi = \frac{C_{soluble} \cdot H \cdot Q_{air}}{C_{soluble} + C_{soluble} \cdot H \cdot Q_{air} + C_{soluble} \cdot K_d \cdot SS} = \frac{H \cdot Q_{air}}{1 + H \cdot Q_{air} + K_d \cdot SS} \quad \text{(Eq.1)}$$

Considering about the typical aeration rate and the Henry coefficient of selected PPCPs, the removal for ADBI due to volatilization is quite significant, but is negligible for pharmaceuticals, estrogens, AHTN, and HHCB.

3.2 Sorption

Solid-Water distribution coefficient is commonly used to determine the fraction of PPCPs sorbed onto sludge. If a solute is introduced into any two phase system, such as soild/water, distribution coefficient (K_d, L/kg) is calculated as the ratio of the concentration of the PPCPs in one phase to the concentration of the PPCPs in the other phase under equilibrium conditions (Eq.2) (Ternes et al. 2004)

$$K_d = \frac{C_{sorbed}}{SS \cdot C_{soluble}} \quad \text{(Eq.2)}$$

where C_{sorbed} is the sorbed PPCP concentration onto sludge (μg/L), $C_{soluble}$ the dissolved concentrate on of the compound (μg/L) and SS the suspended solids concentration (kg/L).

There are two main sorption mechanisms influenced by distribution coefficient:

- *Absorption*: a process in which molecules enter some bulk phase. It refers to the hydrophobic interactions of the aliphatic and aromatic groups of a compound with the lipophilic cell membrane of the microorganisms and the lipid fractions of the sludge. The lipophilicity of substances is related to the octanol-water partition coefficient (K_{ow}). Polycyclic musk fragrances (galaxolide, tonalide, and Celestolide) are the most common lipophilic compounds among PPCPs.

- *Adsorption*: it is the process of accumulating substances that are in solution on a suitable interface. Electrostatic interactions of positively charged groups of chemicals with the negatively charged surfaces of the microorganisms force ions and molecules to bind on the surface or another molecule. Therefore, the tendency of a substance to be ionized or dissociated will influence the efficiency of adsorption. The degree of ionization or dissociation could be characterized by dissociation constant (K_a). In general, cationic species of PPCPs will be more intend to be adsorbed due to Van der Waals interactions, and negatively charged molecules will not be adsorbed.

The sorption coefficient ($K_{d)}$, pseudo first-order degradation constant (k_{biol}), and octanol-water partition coefficient (K_{ow}) values of emerging contaminants frequently found in wastewater treatment plants are given in Table 3.

According the statement above, both octanol-water partition coefficient (Kow)and dissociation constant (K_a) could affect the sorption intendancy of PPCPs. Comparing the properties of selected PPCPs, several phenomena could be illustrated as following: (1) Polycyclic musk fragrances (HHCB, AHTN, ADBI) have high log K_d values (33.3-3.9), which consist with their low solubility in water. The strong lipophilic character could be indicated by high log K_{ow} values (4.6-6.6). (2) Compared with musk fragrances, the selected hormones in Table 3 have both lower log K_{ow} values (2.8-4.2) and sorption coefficients (log K_d of 2.3-2.6). Therefore, they have weaker interaction with sludge. (3) The sorption capacity of the antibiotic trimethoprim (TMP) is similar to that of the previously cited hormones, although in this case the interaction with sludge is mainly driven by adsorption, since this compound is not lipophilic, but at circumneutral pH the dicationic species of TMP

Table 3. Sorption coefficient K_d and degradation rate constant k_{biol} of emerging contaminants in the environment

Compounds		log K_d		log K_{ow}	k_{biol}
		Primary sludge	Biological Sludge		
Galaxolide	HHCB	3.7	3.3	5.9-6.3	<0.03
Tonalide	AHTN	3.7	3.4	4.6-6.4	<0.02
Celestolide	ADBI	3.7	3.9	5.4-6.6	
Diclofenac	DCF	2.7	1.2	4.0-4.5	<0.1
Ibuprofen	IBP	<1.3	0.9	3.5-4.5	9-35
Naproxen	NPX			3.2	0.4-1.9
Fluoxetine	FLX			4.05	
Citalopram	CTL			2.9-3.7	
Estrone	E1		2.4-2.9	3.1-3.4	200-300
17β- estradiol	E2		2.4-2.8	3.9-4.0	300-800
17α- ethinylestradiol	EE2	2.4	2.5-2.8	2.8-4.2	7-9
Diazepam	DZP	1.6	1.3	2.5-3.0	<0.03
Carbamazepine	CBZ	0.09	0.1	2.3-2.5	<0.01
Sulfamethoxazole	SMX		2.3-2.6	0.5-0.9	<0.1
Roxithromycin	ROX		2.3-2.6	2.1-2.8	<0.3
Erythromycin	ERY		2.2	2.5-3.0	0.5-1
Trimethoprim	TMP		2.3	0.9-1.4	
Iopromide	IPM	<0.7	1.0	-2.33	1-2.5

Kow, octanol-water partition coefficient; Kd, sludge-water distribution coefficient; kbiol, pseudo first-order degradation constant (l g-1SS day-1).

Syracuse Research Corporation (www.syrres.com), Kummerer (2000), Stuer-Lauridsen et al. (2000), Jones et al. (2002), Brooks et al. (2003), Ricking et al. (2003), Ternes et al. (2004), Theib (2004), Carballa et al. (2008), Jjemba (2006), Kupper et al. (2006), Ternes and Joss (2006), and Vasskog et al. (2006)

account for approximately 50% of the total TMP concentration (Suarez et al. 2008). Experimental data on PPCPs concentration in sludge are very rare. The possible reason of that could be the difficulty of analysis these compounds precisely in sludge. To overcome this problem, distribution coefficient (K_d) seems to be a useful tool to predict distribution between solid and water phases. However, since K_d is influenced wastewater farm by several parameters, such as the characteristics of the solid phase (organic carbon content, particle size), and experimental conditions in which sorption is studied (sorbate and sorbent concentrations, pH, salinity, ions content), an accurate determination of this coefficient under several environmental conditions is needed (Carballa et al. 2007).

3.3 Biological degradation

During biological degradation in wastewater treatment plants, pharmaceutical contaminants may be transformed into either more hydrophobic compounds, which could be adsorbed onto the solid surface of the activated sludge, or more hydrophilic compounds, which remain in the liquid phase and will eventually be discharged into aquatic environment.

Even there are various groups of microorganisms in the activated sludge, it is unlikely that pharmaceuticals present as microcontaminants in wastewater can be effectively removed by biodegradation alone for three reasons. First, compared with other pollutants in wastewater, pharmaceutical contaminants have relatively low concentration, which may be insufficient to induce enzymes that are capable of degrading pharmaceuticals. Second, since many of the pharmaceutical contaminants are bioactive and this characteristic can inhibit metabolism of microorganisms. As a

result, it is impossible that pharmaceutical contaminants can be used as favorable carbon or energy sources by microorganisms. Third, the nature of each compounds and the operating condition of wastewater treatment plant will influence the performance of biodegradation.

Joss et al. (2006) conveyed a research using activated sludge to investigate the biodegradation of 25 pharmaceuticals, hormones and fragrances , including antibiotics, antiphlogistic, contrast agent , lipid regulator, and nootoropics, in batch experiments at typical concentration levels in a municipal wastewater treatment. He indicated that only a few compounds, which were ibuprofen, paracetamol, 17β-estradiol, and estrone, could be degraded by more than 90%, while half of the target compounds were removed by less than 50%. Joss also determined pseudo first-order degradation kinetics (k_{biol}) for all target compounds down to ng/L levels. Figure 3 shows the degradation constant (k_{biol}) of 35 PPCPs observed in Joss's study. According to the degradation constant (k_{biol}) of target compounds, the contaminants could be divided into three groups: (1) highly degradable, with k_{biol}>10 $Lg^{-1}SSday^{-1}$, such as paracetamol; (2) hardly degradable, with k_{biol}<0.1 $Lg^{-1}SSday^{-1}$, such as carbamazepine; (3) moderate degradable, with 0.1 < k_{biol}<10 $Lg^{-1}SSday^{-1}$, such as iohexol.

4. Biological treatment

4.1 Activated Sludge Process

Full-scale conventional activated sludge process (CAS) is the widest biological treatment technology applied in large urban area. Carballa et al. (2004) conveyed a study researching the removal efficiency of pharmaceuticals, cosmetics, and hormones in a municipal wastewater treatment plant. The researchers indicated that

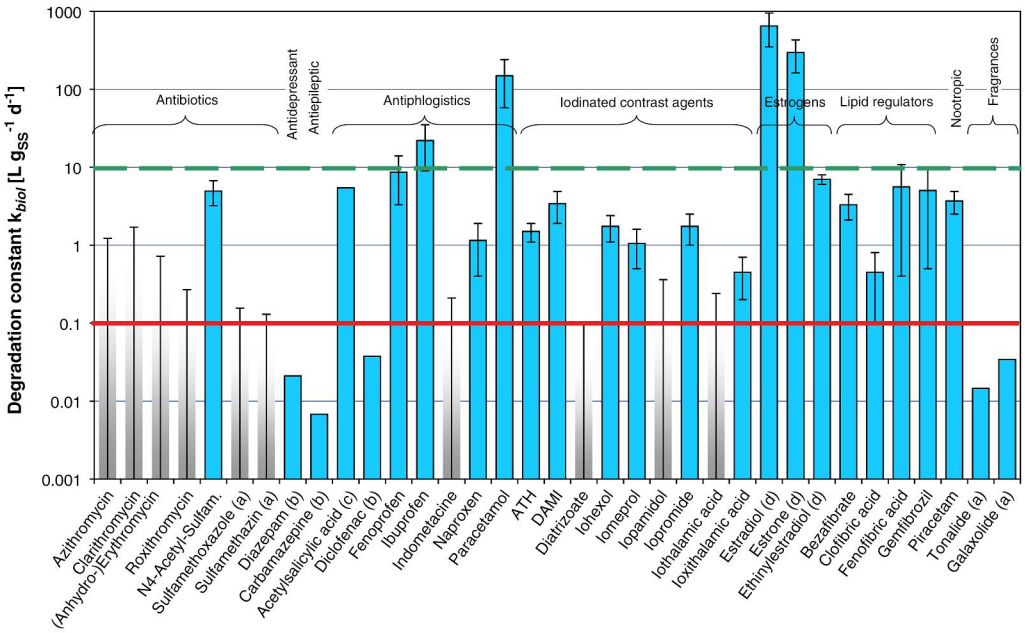


Figure 3. Kinetic degradation constant of 35 pharmaceuticals, hormones, and personal care products. (Joss et al. 2006)

although during the primary treatment process, target compounds were not removed efficiently (ranged from 20 to 50%), the aerobic activated sludge process caused a significant reduction in all compounds detected, between 30 and 75%, with exception of iopromide, which remained in the aqueous phase. The overall removal efficiencies of a wastewater treatment plant could achieve 80% for galaxolide and 83% for tonalide; 65% for ibuprofen, 50% for naproxen, approximately 65% for 17β-estradiol, and 60% for sulfamethoxazole.

Joss et al. (2005) observed no evident correlation between the compound structure and biological removal efficiency. The observed biological removal varied strongly from compound to compound. Galaxolide and tonalide were mainly removed by sorption onto sludge with removal efficiencyiy at least 50%. Ibuprofen is often removed beyond the quantification limit (>90%); naproxen also shows significant removal (50–80%). Partial removal was seen for diclofenac (20–40%). Finally, no removal was seen for Carbamazepine, which consists with other researches (Vieno et al. 2007; Clara et al. 2005).

Contradictory results are documented in literature for the analgesic drug diclofenac. Joss et al. (2005) and Clara et al. (2005) report no significant elimination of diclofenac. In contrast, Ternes et al. (1998) observed elimination rates of up to 70%. Removal of diclofenac might partially attributed to the elimination of sludge during primary treatment and an enhanced sorption onto sludge during secondary treatment (log K_d 2.7) with an addition of inorganic salts for phosphorus precipitation (Ternes 1998; Clara et al. 2005a). The biological degradation of diclofenac is very low (<0.1 l g SS^{-1} day^{-1}) (Joss et al. 2006).

Ibuprofen exhibits high value of biodegradation kinetic coefficient in range of

9-35 l g SS^{-1} day^{-1}. The hydrophilic nature of this substance makes its sorption onto sludge negligible, which means that the main removal mechanism of ibuprofen is biological degradation. High removal efficiency of ibuprofen (>90%) was confirmed by several researches (Joss et al. 2005; Jones et al. 2006; Nakada et al. 2006; Kreuzinger et al. 2004). Although there are also some lower elimination reported, ranging from 50 to 70% (Carballa et al. 2007; Stumpf et al. 1999)

There are three mechanisms involving in the removal of polycyclic musk fragrances, which are volatilization, sorption, and biodegradation. Volatilization seems to be a minor removal pathway in an aeration tank in the case of HHCB and AHTN, while the fraction of ADBI removed by volatilization could achieve approximately 25% (Suarez et al. 2008). Due to the strong lipophilic characteristic of polycyclic musk, the main removal mechanism is sorption onto sludge. In fact, sorption is the only way for AHTN to be removed (Joss et al. 2005). In the case of HHCB, a certain biological degradation was observed (16–50%) and partially confirmed by the detection of one metabolite, HHCB-lactone (Joss et al. 2005; Kupper et al. 2006). ADBI, the third musk considered, showed a similar behaviour as the other two in Kupper et al. (2006), although there is no available data from other work which could confirm this result. The overall removal efficiency of polycyclic muck fragrances could achieve 50 to 70 %, considering all three removal mechanisms (Carballa et al. 2004; Joss et al. 2005; Kupper et al. 2006)

Concerning hormones, the removal efficiencies of estrone (E1), 17β-estradiol (E2), and 17α-ethinylestradiol (EE2) varied strongly between studies. Different kinds of behaviors were observed. (1) Carballa et al. (2004) observed an increase along a wastewater treatment plant. (2) Clara et al. (2005) indicated that when SRT was

higher than 10 days, natural estorgens could achieve around complete removal. Nakada et al. (2006) observed a high removal rate (80%) of estrone. High removal efficiencies reported for E1, E2 and EE2 in activated sludge treatment were observed in the range of 49–99%, 88–98% and 71–94%, respectively (Andersen et al. 2003; Joss et al. 2004). (3) In contrast, Ternes et al. (1999) indicated that there was no significant removal of hormones.

Joss et al. (2004) observed a dependency of the removal of E1 and EE2 on redox conditions. Redox conditions seem to influence their removal, since most of the elimination of E1 and E2 was reported to already occur in the denitrifying step of a STP, whereas EE2 depletion was only observed during the aerobic process (Andersen et al. 2003). These observations were confirmed by batch experiments, showing that: (1) degradation of E1 and E2 could take place under anaerobic, anoxic and aerobic conditions, but at significant different rates (Joss et al. 2004); (2) oxidation of E2 is faster than of E1; and (3) only under aerobic conditions could EE2 be significantly removed and at slower rates than natural estrogens. (Suarez et al. 2008)

Although there is still no certain research indicating the explanation of these deviations, some observation can still be made (Suarez et al. 2008). (1) Different temperature of operation might influence removal efficiency (Ternes et al. 1999). (2) Since E2 is almost completely oxidized to E1, the further oxidation of E1 is slower, and EE2 is appreciable removed even after 48 hours (Ternes et al. 1999a). As a result, a minimum hydraulic retention time is needed to accomplish the complete removal of hormones. (3) The conjugated fractions present in the raw influent of STPs could affect removal performance, since it is not clear where deconjugation occurs.

High removal rates were observed with increasing SRT, and the trend was most

obvious for ibuprofen, bisphenol – A and estrogen. A possible explanation for the high removal rates of ibuprofen is elimination in the form of metabolization of hydroxylibuprofen and carboxyl-ibuprofen (Strenn et al., 2004; Clara et al., 2004). In contrast, the low elimination rate and even the increase in concentration were observed for diclofenac and carbamazepine. Ibuprofen has a high k_{biol} which is consistent with the numerous observations (Joss et al., 2005; Jones et al., 2006; Nakada et al., 2006; Clara et al., 2004) of its efficient removal. Carbamazepine and diclofenac are rarely removed wastewater treatment process due to their poor biodegradation performance and negligible sorption. Moreover, in some researches, the concentration of carbamazepine increased during treatment procedure when SRT was longer than 10 days (Kreuzinger et al., 2004; Clara et al., 2004; Strenn et al., 2004). The most probable explanation for this is conversion of carbamazepine glucuronides and other conjugated metabolites to the parent compound by enzymatic processes in the treatment plant (Vieno et al., 2007). Joss et al. (2005) indicated that the mainly removal mechanism of musk fragrances, galaxolide and tonalide, is expected due to their sorption to the sludge, but not biodegradation.

To sum up, according to the k_{biol} and K_d values of selected PPCPs, the behaviors of these compounds in biological treatment could be distinguished into four categories (Suarez et al. 2008): (1) Compounds with high k_{biol} and low K_d values, such as ibuprofen, could be almost totally removed through biological degradation, regardless of SRT and HRT. (2) Compounds with low k_{biol} and low K_d values, such as carbamzepine, could not be removed nor biotransformed independently of SRT and HRT. (3) Compounds with high k_{biol} and medium K_d values, such as E2 and E1, are moderately transformed slightly dependant on SRT. (4) Compounds with low k_{biol} and

high K_d values, such as musk fragrances, are removed in the aeration tank by sorption and significantly transformed by biological degradation when the SRT is long enough (>10 days).

4.2 Sludge Treatment

Contradictory observations of PPCPs removal during sludge anaerobic digestion are observed. Some authors indicated that PPCPs show some resistance to anaerobic biodegradation. For example, Khan and Ongerth (2002) concluded that most of the compounds in their research (20 pharmaceuticals and 2 of their metabolites) exhibited some resistance to anaerobic degradation. The explanation could be that once digested, sludge solids did not retain their lipophilic properties; as a result, all of the target compounds had partitioned to the aqueous phase. Matsui et al. (2000) observed that 17β-estradiol concentrations and estrogen activity of the dewatering liquid from the sludge treatment were higher than those of the influent to the plant. Anderson et al. (2003) indicated that the inlet and outlet concentrations of estrogens (estrone, 17β-estradiol, and 17α-ethinylestradiol) were similar in an anaerobic digester, concluding that estrogens were not degraded efficiently under methanogenic condition. Johnson and Williams (2004) reported that strictly anaerobic desulphating strains are capable of cleaving estrone-3-sulphate and 17β-estradiol-3-sulphate, thus increasing the concentrations of the corresponding parent compounds (estrone and 17β-estradiol) during this step.

In contrast, opposite results are observed by other authors. For example, Holbrook et al. (2002) indicated that between 51 and 67% of the estrogenic activity contained in the influent wastewater was either biodegraded through wastewater

treatment process (conventional activated sludge with nitrogen and phosphorus removal) or biological sludge treatment processes (mesophilic anaerobic digestion or thermophilic followed by mesophilic aerobic digestion). Moreover, an increase in estrogenic activity and biosolid destruction were observed in both anerobic and aerobic digestion. Kreuzinger et al. (2004) concluded that in general with increasing SRT, the biodegradation of PPCPs increased too. The removal efficiency of most compounds (except carbamazepin) could achieve 70 to 90% after 10 days of SRT. Furthermore, anaerobic digestion could accelerate the breakdown of natural estrogens (estrone and 17β-estradiol).

Carballa et al. (2007) conveyed a study investigating the behavior of 13 PPCPs during anaerobic digestion of wastewater sludge at pilot scale plant. Two parallel processes were carried out, one in mesophilic range (37℃) and the other in thermophilic range (55℃). Different SRT (between 6 and 30 days) was used through the experiments. The higher removal efficiencies were achieved over 85% for the antibiotics (SMX and ROX), natural estrogens (E1, E2, and EE2), and naproxen (NPX). Musk fragrances (HHCB and AHTN) and one anti-phlogistics (DCF) were achieved approximately 60% removal efficiency. The removal efficiency of DZP and IBF ranged from 40 to 60%, while 20% for IPM. The result showed that there was no elimination for CBZ.

4.3 Parameters influencing the removal of PPCPs

4.3.1 ASP

The mainly discussed parameters that influence the removal efficiency of PPCPs in biological treatment are sludge retention time (SRT). SRT means the mean

residence time of biomass in the system, which is a function of the growth rate of microorganisms. According to this definition, higher SRTs allow the enrichment of slowly growing bacteria and consequently the establishment of a more diverse biocoenosis with broader physiological capabilities compared to STPs with low SRT. This is why there is a strong correlation between treatment efficiency and SRT (Kreuzinger et al. 2004).

Kreuzinger et al. (2004) conveyed a serious of experiments to investigate the influence of SRT on the removal efficiency of PPCPs in wastewater treatment (Table 4). According to the data, with SRT less than one day, no removal of most of the selected compounds was shown. For high loaded system, adsorption to activated sludge is the main removal mechanism in liquid phase. However, when the hydraulic detention time is too low for adsorption to reach equilibrium condition, the maximal possible adsorption may not be reached.

For natural estrogens (E1, E2, EE2), high removal efficiency is observed with increasing SRT over 10 days. Since the main removal mechanism of polycyclic musk fragrances is sorption onto sludge, it is expected that the removal efficiency of these compounds will increase with longer SRT. Due to its poor rate of biodegradation as well as its negligible sorption, carbamazepine, an antiepileptic drug, is not well removed regardless of the SRTs. In fact, several researches show the observation of higher concentrations during wastewater treatment processes (Clara et al., 2005b; Vieno et al., 2007; Clara et al., 2004; Kreuzinger et al., 2004). Clara et al. (2004) observed almost twice as high concentrations of carbamazepine in the effluent at $SRT_{10°C}$ higher than 19 days. Also rates of removal of carbamazepine are strongly variable in the activated sludge process. For diclofenac, No trend suggesting

improved removal with increasing SRT was observed.

Although enhanced removal is not observed for all PPCPs investigated with increasing the SRT and no plausible explanation is given for the diverseness in the observed removal of several substances, in general, biological degradation of the PPCPs was enhanced with increasing the SRT. This is also valid if the substance is degraded only as co-substrate, because the SRT necessary for the degradation of the primary substrate is the relevant parameter (Kreuzinger et al., 2004). Moreover, some studies showed that PPCPs could be removed significantly by combining biological treatment process with other wastewater treatment procedures, such as ozonation. Okuda et al. (2008) showed that ozonation process followed by biological treatment could significantly decrease PPCPs investigated including persistent compounds.

Comparison of the results of several different researches is summarized in Appendix C. The fact that enhanced removal could be achieved by raising SRT up over 10 days is observed in these studies.

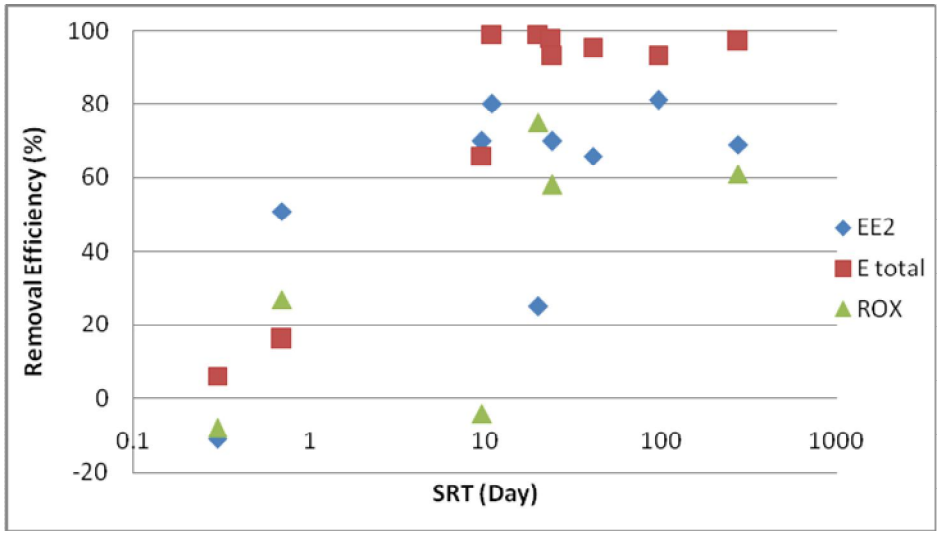
Table 4. Removal of selected PPCPs in wastewater treatment at 20℃ (Kreuzinger et al. 2004)

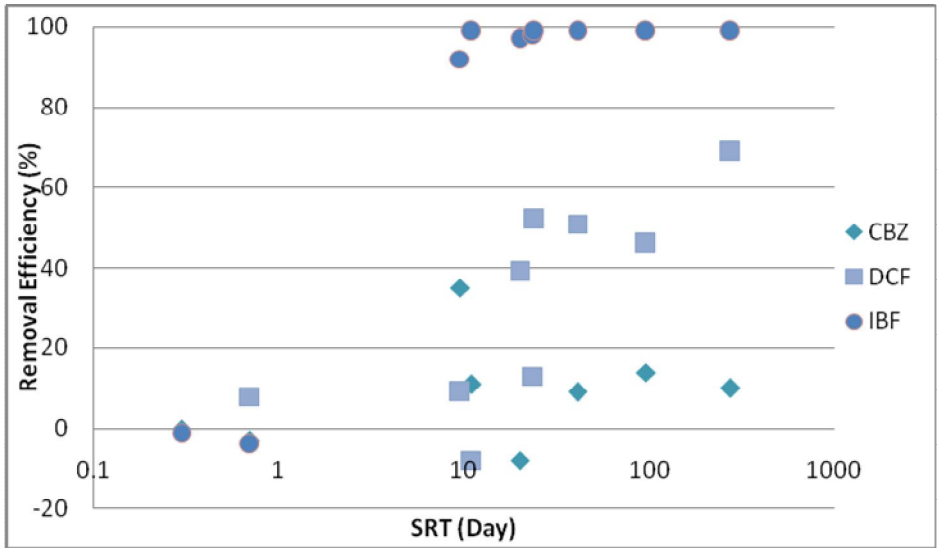
Type	Size	SRT	EE2	E1+E2 +EE2	ROX	SMX	CBZ	DZP	DCF	IBF	IPM	HHCB	AHTN
CAS[a]	WWTP[b]	0.3	-11	6	-8	NA	0	NA	NA	-1	-8	2	-2
CAS	WWTP	0.7	51	16	27	NA	-3	0	7.9	-4	0	27	6
CAS	WWTP	9.6	70	66	-4	NA	35	NA	9	92	50	56	67
Membrane	Pilot plant	11	80	99	NA	57	11	NA	-8	99	NA	85	85
Membrane	Pilot plant	20	25	99	75	33	-8	NA	39	97	NA	90	92
CAS	WWTP	23.6		98	NA	NA	NA	NA	13	98	NA	44	68
CAS	WWTP	24	70	93	58	NA	NA	25	52	99	25	85	90
Membrane	Pilot plant	41	66	95	NA	62	9	NA	51	99	NA	92	91
CAS	WWTP	96	81	93	NA	NA	14	20	46	99	NA	86	87
CAS	WWTP	275	69	97	61	NA	10	23	69	99	NA	89	86

a = conventional activated sludge system

b = wastewater treatment plant

NA = no avalible data





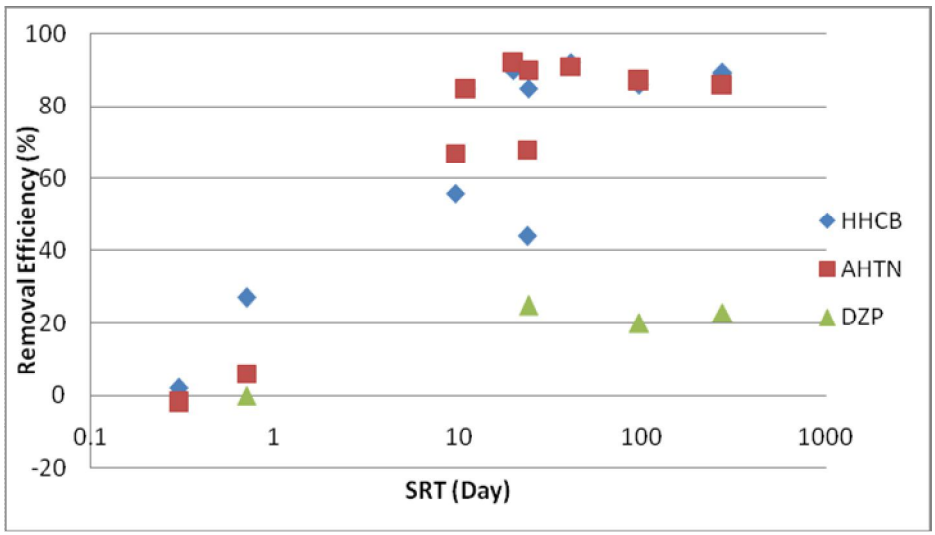


Figure 4. Overall removal efficiency of selected PPCPs in Table 4

4.3.2 Sludge treatment

The main factors which could affect anaerobic biotransformation are biomass adaptation, SRT, temperature and pre-treatment (Carballa et al. 2006). In general, there is no observation of the influence of SRT and temperature on PPCPs removal. The use of pre-treatments (alkaline, thermal and ozonation) cause only minor influence on the removal of PPCPs, and comparing with the absence of elimination observed in the conventional process, only the ozonation process led to some removal of carbamazepine (up to 60% in thermophilic range) (Suarez et al. 2008).

4.3.3 Treatment system

Different conclusions of the influence of treatment system were made. Some researchers indicated that MBR provided better removal of PPCPs than conventional activated sludge treatment. Kimura et al. (2005) reported that improved removal of several pharmaceuticals, ketoprofen, and diclofenac was observed in MBR compared with CAS. Wever et al. (2007) also indicated that 1,6- and 2,7-naphthalene disulfonate had better remove efficiency while treated by MBR. However, there was no better removal of diclofenac observed in Wever's report. Clara et al. (2005) reported that for substances which can reach more than 90% removal rate, only slight differences in the effluent concentration were detected between conventional activated sludge wastewater treatment and membrane bioreactors. This observation leads to that since the contaminant size is at least 100 times smaller than the pore size of the membrane, the major removal mechanism, size exclusion, of MBR does not affect the removal efficiency of PPCPs. An explanation for why MBRs seem to provide higher removal efficiency of micropollutants is that MBR is operated with

longer SRTs than CAS. As mentioned earlier, elimination of PPCPs was mainly attributed to biodegradation due to their chemical properties. Longer SRTs allow for the slow growing bacteria to be retained, and eventually the bacterial population may become enriched to enhance the elimination of PPCPs. According to Appendix C, In general, MBR is operated with longer SRT and showed almost same performance compared to conventional activated sludge treatment.

Nevertheless, MBR offer several advantages compared to conventional systems. First, the membrane allows the detention of particulate matter leading to an effluent free of suspended solids. Second, the emission of contaminants for MBR is lower than conventional systems. Third, MBR reach high SRT in the compact reactor volumes, which could be an advantage of MBR especially in regions without proper receiving water and with water reuse purpose.

5. Conclusion

Although there are still a lot of unknown issues about the biological degradation of EDCs and PPCPs along wastewater treatment plants, a number of conclusions could be drawn:

I. PPCPs have been reported to be present in different environmental water compartments all over the world, such as rivers, lakes, groundwaters and, especially, wastewaters. However, until nowadays, there is no certain legislation for regulating and monitoring these emerging contaminants.

II. The sorption behavior of emerging contaminants in STPs can be predicted by K_d value. Most of the PPCPs show low K_d values, which suggest that instead of sorption, the main removal mechanism of PPCPs in biological treatment is

biodegradation.

III. Biological transformation of PPCPs is not only a function of their biodegradation rate constants (k_{biol}), but also on their solid–water distribution coefficient (K_d). When the SRT of an activated sludge process is long enough, compounds with significant K_d values can be removed through biological degradation. However, once HRT of SRT exceeds certain limit, there is no more removal efficiency enhancing.

IV. Typical wastewater treatment plants are able to achieve high removal efficiency for a limited number of emerging contaminants in present conventional biological treatment plants. AHTN, HHCB, and ADBI could be efficiently removal through sorption onto sludge, and Ibuprofen, estrone, and 17β-estradiol could be removed through biotransformation. Some compounds show remarkable persistent behavior which are unable to be removed through neither sorption nor biotransformation, such as carbamazepine. As a result, most of the present treatment plants can not remove these compounds, so there compounds are continuously discharged in the environment.

V. The exiting researches mainly study the fate of emerging contaminants in the liquid phase. However, since a significant fraction of these substances could be sorbed onto sludge, it is important to understand the behavior of lipophilic substances, such as musk fragrances, EE2, etc.

VI. High removal rates of PPCPs have been reported for membrane bioreactors (MBRs), but the observations noted in this thesis suggest that the improved removals are associated with higher SRTs, but not the process configuration. Most MBRs are operated at high SRT, whereas many activated sludge plants are

operated at low SRT.

6. Furture research needs

To establish safe exposure limits of emerging contaminants in water, a great information is needed to investigate and understand the relevance of trace EDCs and PPCPs in water, and the efficient removal mechanisms of each compound. In addition, since many of emerging contaminants are bioaccumulative, more researches are needed to be done about the toxicological impacts of trace level EDCs and PPCPs in water. As long as the impacts are quantified, safe exposure limits can be established. With adding these limits into water regulation, industries using emerging contaminants will have criteria to follow when they deal with wastewater that they produce. Analytical methods for detection commonly occurring EDCs and PPCPs are also needed to be standardized. The methods commonly used nowadays are based on a few equipment, such as GC/MS and LC/MS. However, the operation and the capital cost of the equipment are too costly and only restricted to several laboratories. The analytical method should be based on equipment that most laboratories could afford and have expertise to operate. Once the analytical methodologies are set up, environmental monitoring of emerging contaminants should include testing for bioaccumulation of EDCs and PPCPs in wildlife and humans. Future studies should also focus on indentifying the relation between emerging contaminants and biomarkers, and population-level impacts of EDCs and PPCPs.

Although reports of EDCs and PPCPs removal by wastewater treatment are beginning to become available, much of the fate of these emerging contaminants in water treatment plant is still unknown. To accuracy assess the removal efficiency of

emerging contaminants across conventional water treatment plants, it is important to understand the distribution of EDCs and PPCPs and their interaction with other contaminants in water, such as heavy metals, nutrients, and other colloidal materials.

Appendix A. Properties of common pharmaceuticals, hormones, and cosmetic ingredients reported in researches

Name	Chemical formula	CAS number	Application	Scientific name
Paracetamol	$C_8H_9NO_2$	103-90-2	Analgesic	N-(4-hydroxyphenyl)acetamide
Metformin hydrochloride	$C_4H_{12}ClN_5$	1115-70-4	Antihyperglycaemic	2-(N,N-dimethylcarbamimidoyl)guanidine hydrochloride
Amoxycillin	$C_{16}H_{19}N_3O_5S$	26787-78-0	Antibiotic	6-[[2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid
Sodium valproate	$C_8H_{15}NaO_2$	1069-66-5	Anti-epileptic	sodium 2-propylpentanoate
Sulphasalazine	$C_{18}H_{14}N_4O_5S$	599-79-1	Antirheumatic	(3Z)-6-oxo-3-[[4-(pyridin-2-ylsulfamoyl)phenyl]hydrazinylidene]cyclohexa-1,4-diene-1-carboxylic
Mesalazine (systemic)	$C_7H_7NO_3$	89-57-6	Treatment of ulcerative colitis	5-amino-2-hydroxy-benzoic acid
Ferrous sulphate	FeO_4S	7782-63-0	Iron supplement	iron(+2) cation sulfate
Ranitidine hydrochloride	$C_{13}H_{23}ClN_4O_3S$	66357-59-3	Anti-ulcer drug	N-[2-[[5-(dimethylaminomethyl)-2-furyl]methylsulfanyl]ethyl]-N'-methyl-2-nitro-ethene-1,1-diamine hydrochloride
Cimetidine	$C_{10}H_{16}N_6S$	51481-61-9	H2 receptor antagonist	3-cyano-2-methyl-1-[2-[(5-methyl-1H-imidazol-4-yl)methylsulfanyl]ethyl]guanidine
Atenolol	$C_{14}H_{22}N_2O_3$	29122-68-7	b-blocker	2-[4-[2-hydroxy-3-(propan-2-ylamino)propoxy]phenyl]acetamide
Oxytetracycline	$C_{22}H_{24}N_2O_9$	79-57-2	Antibiotic	(2Z)-2-(amino-hydroxy-methylidene)-4-dimethylamino-5,6,10,11,12a-pentahydroxy-6-methyl-4,4a,5,5a-tetrahydrotetracene-1,3,12-trione
Diclofenac sodium	$C_{14}H_{10}Cl_2NNaO_2$	15307-79-6	Anti-inflammatory and Analges	sodium 2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetate
Flucloxacillin sodium	$C_{19}H_{18}ClFN_3NaO_6$	1847-24-1	Antibiotic	sodium (2S,5R,6R)-6-[[3-(2-chloro-6-fluoro-phenyl)-5-methyl-oxazole-4-carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-

Name	Chemical formula	CAS number	Application	Scientific name
Phenoxymethylpenicillin	$C_{16}H_{18}N_2O_5S$	87-08-01	Antibiotic	(2S,5R,6R)-3,3-dimethyl-7-oxo-6-[(2-phenoxyacetyl)amino]-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid
Allopurinol	$C_5H_4N_4O$	315-30-0	Antigout drug	2,4,8,9-tetrazabicyclo[4.3.0]nona-1,3,6-trien-5-one
Diltiazem hydrochloride	$C_{22}H_{27}ClN_2O_4S$	33286-22-5	Calcium antagonist	[(3S,4S)-6-(2-dimethylaminoethyl)-3-(4-methoxyphenyl)-5-oxo-2-thia-6-azabicyclo[5.4.0]undeca-7,9,11-trien-4-yl] acetate hydrochloride
Gliclazide	$C_{15}H_{21}N_3O_3S$	21187-98-4	Antihyperglycaemic	3-(7-azabicyclo[3.3.0]oct-7-yl)-1-(4-methylphenyl)sulfonyl-urea
Aspirin	$C_9H_8O_4$	50-78-2	Analgesic	2-acetyloxybenzoic acid
Quinine sulphate	$C_{40}H_{50}N_4O_8S$	804-63-7	Muscle relaxant	(R)-[(5S,7S)-5-ethenyl-1-azabicyclo[2.2.2]oct-7-yl]-(6-methoxyquinolin-4-yl)methanol; sulfuric acid
Mebeverine hydrochloride	$C_{25}H_{36}ClNO_5$	3625-06-7	Antispasmodic	4-[ethyl-[1-(4-methoxyphenyl)propan-2-yl]amino]butyl 3,4-dimethoxybenzoate hydrochloride
Mefenamic acid	$C_{15}H_{15}NO_2$	61-68-7	Anti-inflammatory	2-[(2,3-dimethylphenyl)amino]benzoic acid
Galaxolide (HHCB)	$C_{18}H_{26}O$	1222-05-5	Fragrance	1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-hexamethyl-cyclopenta-gamma-2-benzopyran
Tonalide (AHTN)	$C_{18}H_{26}O$	1506-02-1	Fragrance	1-(3,5,5,6,8,8-hexamethyltetralin-2-yl)ethanone
Celestolide (ADBI)	$C_{17}H_{24}O$	88401-65-4	Fragrance	1-(1,1-dimethyl-6-tert-butyl-2,3-dihydroinden-4-yl)ethanone
Diclofenac (DCF)	$C_{14}H_{11}C_{l2}NO_2$	15307-86-5	Anti-inflammatory	2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetic acid
Ibuprofen (IBP)	$C_{13}H_{18}O_2$	15687-27-1	Anti-inflammatory	2-[4-(2-methylpropyl)phenyl]propanoic acid
Naproxen (NPX)	$C_{14}H_{14}O_3$	22204-53-1	Anti-inflammatory	2-(6-methoxynaphthalen-2-yl)propanoic acid
Fluoxetine (FLX)	$C_{17}H_{18}F_3NO$	59333-67-4	Anti-depressants	N-methyl-3-phenyl-3-[4-(trifluoromethyl)phenoxy]propan-1-amine

Name	Chemical formula	CAS number	Application	Scientific name
Citalopram (CTL)	C20H21FN2O	59729-33-8	Anti-depressants	1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-3H-isobenzofuran-5-carbonitrile
Estrone (E1)	C18H22O2	53-16-7	Estrogens	1,3,5(10)-Estratrien-3-ol-17-one
17β- estradiol (E2)	C18H24O2	50-28-2	Estrogens	1,3,5-Estratriene-3,17b-diol
17α- ethinylestradiol (EE2)	C20H24O2	57-63-6	Estrogens	17a-Ethynyl-1,3,5(10)-estratriene-3,17b-diol
Diazepam (DZP)	C16H13ClN2O	439-14-5	Tranquillizers	7-Chloro-1-methyl-5-phenyl-3H-1,4-benzodiazepin-2(1H)-one
Carbamazepine (CBZ)	C15H12N2O	298-46-4	Antriepileptics	5H-dibenz[b,f]azepine-5-carboxamide
Sulfamethoxazole (SMX)	C10H11N3O3S	723-46-6	Antibiotics	4-Amino-N-(5-methyl-3-isoxazolyl) benzenesulfonamide
Roxithromycin (ROX)	C41H76N2O15	80214-83-1	Antibiotics	Erythromycin 9-(-O-[2-methoxyethoxy] methyloxime)
Erythromycin (ERY)	C37H67NO13	114-7-8	Antibiotics	6-(4-Dimethylamino-3-hydroxy-6-methyl-tetrahydro-pyran-2-yloxy)-14-ethyl-7,12,13-trihydroxy-4-(5-hydroxy-4-methoxy-4,6-dimethyl-tetrahydro-pyran-2-yloxy)-3,5,7,9,11,13-hexamethyl-
Trimethoprim (TMP)	C14H18N4O3	738-70-5	Antibiotics	2,4-Diamino-5-(3,4,5-trimethoxybenzyl) pyrimidine
Iopromide (IPM)	C18H24I3N3O8	73334-07-3	X-ray contrast media	N,N-bis(2,3-dihydroxypropyl)-2,4,6-triiodo-5-(2-methoxyacetamido)-N-methylisophtalamide

Appendix B. Charateristics of the treatments

Ref#	Author	Location	Plant (Type, SRT)	Size, HRT,PE(*10^3)	Temp,°C	Conclusion
1	Joss et al (2005)	Swiss	WWTP1 - CAS w/MBR, SRT(10~12d)/CAS, 16,33,75d/MBR WWTP2 - CAS w/FBR, SRT(22~24d)/CAS	HRT: CAS(7.3h), MBR(13h), PE = 55 HRT: CAS(16.8h),FBR(0.7h), PE = 80	CAS1: 13~16, MBR: 12~16 CAS2: 12~21, FBR: 12~19	variation of SRT btw 10 and 60-80 days showed no significant impact on the transformation efficiency
2	Jones et al (2006)	South England	1 STP - CAS SRT(13d)	HRT(13.5h) PE(150)	20.6	removoal effic for all compounds >90%, but conc of hundred nanograms still present
3	Xu et al (2007)	South China	4 STPs 1:CAS, SRT(4.5-6h) 2:Oxidation ditch,SRT(NA),3:CAS,SRT(5.6-8h) 4:chem enhanced,SRT(3-4h)	1: HRT(22h), PE(80),2:HRT(12-18h),PE(1,050) 3:HRT(15-22h),PE(300) 4:HRT(8-12h),PE(3,500)		the removal of antibiotics here was poor. Fluoroquinolones easily absorbed Low removal of macrolides
4	Oppenheimer (2007)	U.S.	6 facilities, SRT ranging from 0.5 to 30 days	Capa: 5-300 MGD		SRT80 (80% removal) for each comp was found. From excellent to poor removal
5	Kreuzinger et al (2004)	Austria	4 WWTPs 1: CAS(1stage), SRT(24,96,275d) 2 CAS(1 stg),SRT(0.7d),3:CAS(1stg),SRT(23.6d) 4:CAS(2 stg),SRT(0.3, 9.6d)	1: PE(7), 2:PE(2,500) 3:PE(135), 4:PE(167)	set as T = 20	Although not all substances are degraded better w/ SRT increases, in general, biodeg rate increases.
6	Clara et al (2004)	Austria	5 WWTPs 1: CAS, SRT(2d) 2:CAS(2 stg+ anaero sludge),SRT(19d) 3:CAS+anaero sludge, SRT(48d) 4:CAS,SRT(100/100/42d),	1: PE(2,500), 2:PE(167) 3:PE(135), 4:PE(6), 5:PE(0.05)	set as T = 10	some of comps dependent on SRT(BPA,IBP,bezafibrate & estrogens -strong correl bet effl conc and SRT),but the antiepileptic drug carbamazepine not affected.
7	Nakada (2006)	Tokyo, Japan	5 STPs w/ activated sludge SRT(d): 3.8, 4.6, 5.8, 5.0, 8.4	Size(MGD): 170,108,85,317,55 HRT(h): 8.6,8.0,9.4,7.1,8.9 PE: 709,731,764,2020,464	Samples collected seasonally	Good removal: Aspirin,ibuprofen,and thymol Poor removal: amide-type pharmaceuticals (crotamiton,carbamazepine),ketoprofen and naproxen thymol(high vapor pressure), estrogens well removed
8	Vieno et al (2007)	Finland	12 STPs w/ CAS mostly SRT(d) 2 to 20 variously	Size(MGD): 0.2 - 62 HRT(h): 1.5 - 20 PE: 2.4 - 740	the effect of temp cannot be assessed (same season collected)	no elimination:carbamazepine, poor(<40%): metoprolol moderate(40-80%): acebutolo,atenolo,,sotalol efficient(>80%): ciprofloxacin, norfloxacin,ofloxacin
9	Hashimoto et al (2007)	Japan	10 WWTPs w/ CAS SRT(d): 2-10	Size(MGD): 1.5 - 9.9 HRT(h): 6 - 26 PE: 16 - 131	Summer: 20 - 28 Winter: 13 - 25	E2 & E3: effectively removed, E1: poor removal because E2 quickly converted to E1 & degradation rate of E1 is less than E2(decrement of E2,increment of E1)

Ref#	Author	Location	Plant (Type, SRT)	Size, HRT,PE(*10^3)	Temp,°C	Conclusion
10	Batt et al (2007)	U.S.	3 WWTPs w/ activated sludge SRT(d); 1 WWTP (6 and 49 for stg 1 and 2 respectively) 15,17 for other two WWTPs	Size(MGD): 0.8,4.5 and 30 HRT(h): 1 - 4		SRT is important in the 2nd tratment process that influences the reduction of antibiotics. But chemical degradation via chlorine disinfection can contribute to the removal of several antibiotics is susceptible
11	Batt et al (2006)		Batch experiment & one WWTP: stage1(CAS) w/SRT(6d) stage2(CAS w/ nitrif) w/ SRT(49d)	Size(MGD): 30 HRT(h):1,2		The removal rates of iopromide and trimethoprim w/ nitrification is higher than the removal rates w/o nitrification. these nitrifying bacteria play a key role in the biodegradation w/ high SRT(nitrification)
12	Kimura et al (2007)	Japan	1 WWTP (SRT:7d) 2 MBRs (SRT:15 & 65d)	Size(MGD): 1WWTP (33) 2 MBRs	summer(Aug - Oct)	high removal w/ longer SRTs: ketoprofen and diclofenac ibuprofen is always highly removed. MBR w/ longer SRT showed better performance
13	Radjenovic et al (2007)	Spain	Lab - scale MBR compared with removal in CAS SRT of MBR was set infinite because of no sludge discharged from the reactor SRT of CAS w/ nit (d):3	CAS system w/ nit of WWTP Size(MGD): 5.8 HRT(h): 14		MBR eff conc were significantly lower than eff from CAS. Despite of MBR lab-scale exp & real CAS, it shows that longer SRT means better removal efficiencies.
14	Clara et al (2004)	Austria	1 STP(CAS) SRT: 91, 275, 21 1 MBR SRT: 11, 41, 20d	PE: 7	set T = 20	No significant differences between the removal rates in the CAS and MBR were observed.The biological degradation is dependent on the SRT.
15	Strenn et al (2004)	Austria	12 SWPs SRT: 1,4,17,29d		set T = 20	Clear dependency on SRT for Bezafibrate, whereas the removal rates for Ibuprofen are varying. No removal for Carbamazepine. The results of Diclofenac vary vigorously
16	Clara et al (2005)	Austria	1 MBR (SRT: 10,27,55d) 3 WWTPs: WWTP1 (SRT: 114,237,52d) WWTP2(SRT: 2d), WWTP3(SRT: 46d)		Samples collected seasonally	BPA, IBP, BZF are well degraded achieving over 90% removal. UF doesn't allow any further retention of the invstigated substances due to size exclusion.

Appensic C. Removal of PPCPs in relation to the SRTs in different wastewater treatments

	SRT Range				
Compond	**< 2d**	**2d - 5d**	**5d -10d**	**10d -20d**	**> 20d**
Carbamazepine (CBZ)	0,-3 at 20°C/Ref5(CAS) 0 at 20°C/Ref15(CAS)	-3 at 10°C/Ref6(CAS) < 45[a] 2 at 20°C/Ref15(CAS)	-44[b] 35 at 20°C/Ref5(CAS)	20,-25,3 at 14,13,16° C/Ref1(CAS) 25,-20,-5 at 15,12,16°	10,-20 at 21,12°C/Ref1(CAS) 9 at 20°C/Ref5(MBR) 14,10 at 20°C/Ref5(CAS)
Diazepam (DZP)					25,20,23 at 20°C/Ref5(CAS)
Diclofenac (DCF)	7.9 at 20°C/Ref5(CAS) 8 at 20°C/Ref15(CAS)	7.1 at 10°C/Ref6(CAS) 50.1/Ref13(CAS w/ nit) 25 at 20°C/Ref15(CAS)	9 at 20°C/Ref5(CAS) 42/Ref12(CAS)	35,20,30 at 14,13,16° C/Ref1(CAS) 35,15,40 at 15,12,16°	35,30 at 21,12°C/Ref1(CAS) 13,52,46,69 at 20°C/Ref5(CAS) 51 at 20°C/Ref5(MBR)
Erythromycin (ERY)	45,15,45/ Ref3(CAS,CAS,chem)	23,8/Ref13(CAS w/ nit)			
Estradiol (E2)		90%[a]	85.7[c]		
Estriol		18 at 10°C/Ref6(CAS) 100%[a]	99.5[c]	26 at 10°C/Ref6(CAS)	100,100,100,100 at 10°C/Ref6(CAS) 100,100,100 at 10°C/Ref6(MBR)
Estrone (E1)		-112 at 10°C/Ref6(CAS) 86[a]	-55.9[c]	84.3 at 10°C/Ref6(CAS)	100,94,100,98 at 10°C/Ref6(CAS) 97,28,100 at 10°C/Ref6(MBR)
Galaxolide (HHCB)	2,27 at 20° C/Ref5(CAS) 38 at 20°C/Ref16(CAS)		56 at 20°C/Ref5(CAS)	60,35,40 at 14,13,16° C/Ref1(CAS) 60,40,30 at 15,12,16°	50,50 at 21,12°C/Ref1(CAS) >30d for SRT80/Ref4 92 at 20°C/Ref5(MBR)
Ibuprofen (IPF)	-1, -4 at 20° C/Ref5(CAS) -4.3 at 10°C/Ref6(CAS)	4.5d for SRT80/Ref4 over 90%[a] 82.5/Ref13(CAS w/ nit)	92 at 20°C/Ref5(CAS) 98/Ref12(CAS) 81 at 20°C/Ref15(CAS)	99,93,98 at 14,13,16° C/Ref1(CAS1) 90,95,95 at 15,12,16°	97,94 at 21,12°C/Ref1(CAS2) 97,99 at 20°C/Ref5(MBR) 98 at 10°C/Ref6(CAS)

	SRT Range				
Compond	**< 2d**	**2d - 5d**	**5d -10d**	**10d -20d**	**> 20d**
Iopromide (IPM)	-8, 0 at 20° C/Ref5(CAS) -32 at 20°		50 at 20°C/Ref5(CAS) -22/Ref11(CAS)	45,30,80 at 14,13,16° C/Ref1(CAS) 40,65,75 at 15,12,16°	92,60 at 21,12°C/Ref1(CAS) 25 at 20°C/Ref5(CAS) 61/Ref11(CAS w/ nit)
Naproxen (NPX)		45%(range: 0-80%)[a] 85.1/Ref13(CAS w/ nit)	64/Ref12(CAS)	75,80 at 13,16° C/Ref1(CAS) 75,80,77 at 15,12,16°	65,70 at 21,12°C/Ref1(CAS) >96/Ref12(MBR)
Roxithromycin (ROX)	65,55,75/ Ref3(CAS,CAS,chem) -8,27 at 20°		-4 at 20°C/Ref5(CAS)	20,40,-20 at 14,13,16° C/Ref1(CAS) 40,60,55 at 15,12,16°	40,5 at 21,12°C/Ref1(CAS) 58,61 at 20°C/Ref5(CAS) -58,44,41,-80 at 20°C/Ref16(CAS)
Sulfamethoxazole (SMX)	35,64/Ref3(ox,chem) -279 at 20° C/Ref16(CAS)	55.6/Ref13(CAS w/ nit)	57/Ref10(Amhest-CAS1	55,55 at 14,13° C/Ref1(CAS) 90,75,70 at 15,12,16°	70,65 at 21,12°C/Ref1(CAS) 33,62 at 20°C/Ref5(CAS) 42/Ref10(Amherst CAS2 w/ nit)
Tonalide (AHTN)	-2,6 at 20° C/Ref5(CAS) 64 at 20°C/Ref16(CAS)		67 at 20°C/Ref5(CAS)	55,25,20 at 14,13,16° C/Ref1(CAS) 50,40,30 at 15,12,16°	40,50 at 21,12°C/Ref1(CAS) 68,90,87,86 at 20°C/Ref5(CAS) 87,83,19 at 20°C/Ref16(CAS)
Trimethoprim (TMP)			-4/Ref10(Amherst CAS1) -1/Ref11(CAS)	97,83/Ref10	68/Ref10(Amherst- CAS2 w/ nit) 50/Ref11(CAS w/ nit)

Ref # : Exhibiting in appendix B
a : avg removal rate for SRT 3.8 to 8.4d (Ref.8)
b : avg removal rate for SRT 2 to 20d (Ref.10)
c : avg removal rate for SRT 2-10 (Ref.11)
CAS : Conventional activated sludge
MBR : Membrane bioreactor
nit : Nitrification
ox : Oxidation ditch

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