Removal Characteristics and Predictive Model of Pharmaceutical and Personal Care Products (PPCPs) in Membrane Bioreactor (MBR) Process

2016

JUNWON PARK

Removal Characteristics and Predictive Model of Pharmaceutical and Personal Care Products (PPCPs) in Membrane Bioreactor (MBR) Process

（膜分離活性汚泥法における残留医薬品類の除去特性と予測モデルの開発）

JUNWON PARK

A Dissertation submitted in partial fulfilment of

the requirements for the degree of

Doctor of Engineering

Department of Urban and Environmental Engineering

Graduate School of Engineering

Kyoto University

Kyoto, Japan

2016

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LIST OF ABBREVIATIONS

APAP: Acetaminophen	ETZ: Ethenzamide	SDMX: Sulfadimethoxine
ANP: Antipyrine	FP: Fenoprofen	SDM: Sulfadimidine
ATL: Atenolol	FSM: Furosemide	SMR: Sulfamerazine
AZM: Azithromycin	GF: Griseofulvin	SMZ: Sulfamethoxazole
BZF: Bezafibrate	IFP: Ifenprodil	SMM: Sulfamonomethoxine
CAF: Caffeine	IND: Indometacin	SP: Sulfapyridine
CBZ: Carbamazepine	IPA: Isopropylantipyrine	STZ: Sulfathiazole
CTC: Chlortetracycline	KTP: Ketoprofen	SLP: Sulpiride
CPFX: Ciprofloxacin	LVFX: Levofloxacin	TC: Tetracycline
CAM: Clarithromycin	LM: Lincomycin	TEP: Theophylline
CLB: Clenbuterol	MFA: Mefenamic acid	TAP: Thiamphenicol
CFA: Clofibric acid	MTL: Metoprolol	TL: Tiamulin
CRT: Crotamiton	NPX: Naproxen	TCC: Triclocarban
CTX: Cyclophosphamide	NFX: Norfloxacin	TCS: Triclosan
DEET: N,N-Diethyl-meta-toluamide	OXT: Oxytetracycline	TRM: Trimethoprim
DCF: Diclofenac	PIR: Pirenzepine	TYL: Tylosin
DTZ: Diltiazem	PRI: Primidone	2QCA: 2_quinoxalinecarboxylicacid
DIP: Dipyridamole	PPL: Propranolol	
DIS: Disopyramide	RXM: Roxithromycin	
ENR: Enrofloxacin	SAL: Salbutamol	

ABSTRACT

Recently, wastewater reclamation is considered as one of the most effective solutions to global water scarcity. However, one of the key issues in wastewater reuse is the emerging problem of micropollutants such as pharmaceutical and personal care products (PPCPs) due to their potential to cause negative effects on aquatic ecosystems. PPCPs are widely employed for human health, cosmetic care, agricultural practice and veterinary medicine, and usually released into water environment. Particularly, the main source of these compounds has been known as the effluent from wastewater treatment plants (WWTPs), but current WWTPs operating usually by conventional activated sludge (CAS) system are only designed for removal of organic matters and nutrients, without considering PPCPs, and thus most of these compounds are not completely removed. On the other hand, membrane bioreactor (MBR) process has become an alternative to CAS processes for removal of PPCPs as well as conventional pollutants in wastewater treatment since higher mixed liquor suspended solids (MLSS) concentration usually developed in MBR can increase the biodegradation potential and adsorption capability. Although some researchers have pointed out the importance of PPCPs removal in wastewater treatment processes, in which occurrence, fate and removal efficiency were extensively studied, there is little knowledge on removal performance and mechanisms of PPCPs in MBR process. Therefore, removal characteristics and mechanisms of target compounds in MBR process were investigated in this study. Furthermore, predictive models were developed based on removal characteristics which can be obtained in MBR process and evaluated by data of practical wastewater treatment.

Firstly, removal fate and efficiency of 57 target compounds in MBR process, with different units in various biological treatment processes were investigated. Analgesics and antibiotics were detected at the highest level, and mass loading rate including stimulant, non-steroidal anti-inflammatory drugs (NSAIDs) and antibacterials accounted for median 85% in the studied WWTPs. Over 92% of PPCPs in influent were efficiently eliminated, indicating better or comparable removal performance to WWTPs of other countries. Biological treatment processes appeared to be most effective in eliminating most PPCPs, while some PPCPs were additionally removed by post treatment which was used for purpose of disinfection. With exception of MBR process, A2O system was found to be effective for PPCPs removal and as a result removal mechanisms were

evaluated by calculating mass balance of A2O and lab-scale MBR process. Comparative study highlighted contribution of biodegradation was highly responsible for the improved removal performance found in lab-scale MBR (e.g., bezafibrate, ketoprofen and atenolol). Triclocarban, ciprofloxacin, levofloxacin and tetracycline were greatly adsorbed onto MBR sludge. Increased biodegradability was also observed in lab-scale MBR process despite of highly adsorptive characteristics, suggesting that enhanced biodegradation potential achieved in MBR process had a key role in eliminating high adsorptive compounds as well as persistent PPCPs in other biological treatment processes.

Secondly, the study regarding removal of PPCPs and fouling control in combination of MBR and coagulation process was evaluated. From the our results, permeability performance increased in accordance with addition of coagulants and membrane fouling significantly reduced due to the attenuated irreversible fouling by decrease of SMP concentration and inorganic matters of cake layer or membrane surface. Moreover, compared with control-MBR, removal of some PPCPs such as ketoprofen, diclofenac, furosemide and sulfamethoxazole was found to be effective in coagulation-MBR with addition of PAC due to increased bioactivity of sludge. It can be proven by the results on comparison of mass balance between two systems, suggesting that increased removal efficiencies could be mostly attributed to the enhanced biodegradability. This study will give useful insights into the applicability of process for sustainable water reuse in terms of not only control of membrane fouling, but also efficient removal of PPCPs.

Thirdly, batch experiments were carried out to elucidate the removal pathways in MBR process by determining the biodegradation and adsorption constant of 45 selected compounds according to different kinetic models, in which removal mechanisms of individual compounds were significantly relevant to classes and categories of PPCPs. Biodegradation and adsorption onto sludge were considered as important factors for eliminating PPCPs, whereas removal via hydrolysis and volatilization seemed to be negligible in MBR process. Regarding comparison between MBR and CAS sludge, highly biodegradable PPCPs was greatly eliminated via biodegradation in MBR compared with CAS. Also, the fate of persistent or non-degradable substances like furosemide, diclofenac, sulfathiazole and DEET in CAS sludge moved from a recalcitrant behavior to a partial removal in MBR sludge, which can be attributed to enhanced biodegradation. On the other hand, no obvious differences on adsorption affinity and mass transfer rate of most PPCPs between in MBR and CAS sludge were observed, suggesting that removal via adsorption was not strongly dependent on the sludge characteristics. Thus, MBR process is not expected to outcompete the CAS

process in terms of removal by adsorption despite high MLSS concentration.

Fourthly, in order to identify the reasons why MBR process can be superior to other kinds of WWTPs, elimination of PPCPs by variations of solids retention time (SRT) was studied. Although highly biodegradable substances such as caffeine, theophylline, fenoprofen and bezafibrate were not dependent on the changes of SRT, removal of some moderate or hardly degradable compounds, such as naproxen, indometacin, furosemide, DEET and 2QCA was significantly attributable to increase of SRT. It demonstrates that MBR process operating at the prolonged SRT can obviously provide conditions more conducive to biodegradation. Moreover, distinct capability of nitrifying bacteria to degrade target compounds was evaluated, in which a wide array of PPCPs were removed via nitrification by ammonia oxidizing bacteria (AOB), thereby improving removal performance in MBR process. Based on the results of cometabolic degradation rates and transformation yields, PPCPs having greater values are able to be highly degraded by cometabolism derived from non-specific enzymes. Furthermore, estimated values were used as valuable parameters for predictive models.

Lastly, operating factors governing removal of PPCPs were identified using Principal component analysis (PCA), in which biodegradation was positively dependent to temperature and MLSS concentration, whereas dissolved oxygen in the bioreactors and residual NO_3-N concentration in effluent were not significantly correlated with removal via biodegradation. Model-based evaluation based on removal pathways was performed to predict removal performance of PPCPs. For bezafibrate, ketoprofen, furosemide and naproxen, predictive model showed a perfect match to observed data in pilot-scale MBR process, suggesting that this model can be practically applied in MBR process to predict elimination of compounds which have a higher biodegradability in accordance with conditions of microorganisms in the bioreactors. In addition, cometabolic model predicted more accurately the removal by cometabolic degradation of several substances compared with pseudo first-order kinetics. The growth of AOB as well as biotransformation by nitrification contributed greatly to the removal of propranolol, diltiazem, sulfathiazole, sulfamethoxazole and lincomycin, for which the variations of not only specific growth rate of AOB, but also microbial populations of AOB can play an important role in enhancing the cometabolic degradation.

Chapter Ⅰ

Introduction

1.1 Research background

It has been known for over 20 years that pharmaceuticals and personal care products (PPCPs) are released into the environment because more than 100,000 chemicals have been used in our everyday life, either in households, agricultures and industries. The PPCPs have been detected in any water body such as river water, ground water and drinking water and thus the presence of PPCPs in the environment has emerged as a societal issue. From several decades ago government and non-government organizations as the European Union (EU), the North American Environmental Protection Agency (EPA) are considering these problems and setting up directives and legal frameworks to protect and improve the quality of fresh water resources, but the studies with respect to exposure and impacts on human health and ecosystem are still evolving (U.S.EPA, 2010).

Moreover, the main source of these compounds has been known as the effluent from wastewater treatment plants (WWTPs) (Halling-Sørensen et al., 1998; Kanda et al., 2003). Numerous literature reviews have pointed out that current WWTPs operating usually by conventional activated sludge (CAS) system are only designed for removal of organic matters and nutrients, without considering PPCPs, and therefore most of these compounds are not completely removed (Carballa et al. 2004; Onesios et al. 2009). Consequently, there has been a growing interest on dealing with efficient removal of PPCPs in WWTPs using advanced treatment processes such as membrane filtration, advanced oxidation process (AOP). Among many kinds of technology, membrane bioreactors (MBR) process, the combination of membrane filtration and biological treatment in mixed liquor, have been widely applied for wastewater reclamation. The global market for MBR systems grew to $838.2 million in 2011 and is projected to

increase up to $3.44 billion by 2018, which represents a compound annual growth rate (CAGR) of 22.4% over this time period (Water and wastewater internationals). Also, MBR has become an alternative to CAS process for efficient removal of PPCPs because it can operate higher mixed liquor suspended solids (MLSS) concentration and longer solids retention time (SRT), leading to enhanced biodegradation potential attributed to microbial activity and diversity and increased adsorption tendency of target compounds. Most of the available scientific studies have suggested that MBR process proved to be better performance than CAS process in terms of removal of PPCPs (Kimura et al., 2005; Terzic et al., 2005; Bernhard et al., 2006; Hu et al., 2007; Miège et al., 2009; Sipma et al., 2010).

However, removal efficiency of PPCPs depends strongly on not only the physicochemical properties and intrinsic nature such as chemical structures, molecular weight, hydrophobicity and electrostatic interaction of each compound, but also operating conditions of WWTPs like hydraulic retention time (HRT), SRT, influent sources, compartment of reactor and water temperature (Joss et al., 2005; Gros et al., 2010; García-Galán et al., 2011).

In addition, since PPCPs are eliminated in biological treatment process by various removal mechanisms like biodegradation, adsorption onto sludge, volatilization and photodegradation, it is very hard to elucidate removal characteristics and pathways of these substances, even though recent studies have focused on the influence on elimination of PPCPs by biological treatment processes including MBR by emphasizing on the identification of the removal routes and even predicting their fate and removal performance using mathematical equations and model parameters (Urase et al., 2005; Joss et al., 2006; Plosz et al., 2010; Pomiès et al., 2013; Fernandez-Fontaina et al., 2013). Overall, up to now, the knowledge on the removal pathways and characteristics in MBR are still limited. Thus, it will be necessary to better understand the reasons why MBR process can obtain improved removal performance than CAS process as well as evaluate predictive model based on removal mechanisms.

1.2 Research objectives

According to the above research background, detailed objectives of this study are as follows:

1) To better understand the fate and removal characteristics of PPCPs in MBR process, with various biological treatment processes of WWTPs
2) To elucidate removal pathways of target compounds and the effect of microbial diversity and composition on removal of PPCPs
3) To develop a predictive model and evaluate practical applicability of the proposed model

1.3 Research structures

This dissertation consists of eight chapters. As can be seen in Figure 1.1, the structure of this research work is described with a general outline of each chapter.

A background of the research with research objectives and structure was described in Chapter I. In Chapter II, a literature review was summarized based on the available knowledge on removal of PPCPs in biological treatment processes including MBR technology, the effect of coagulation, and critical overview on predictive models and parameters.

In Chapter III, target PPCPs were analyzed and compared from the samples of different units (e.g., biological treatment and post treatment processes) in various WWTPs to identify removal fate and characteristics in MBR. Also, comparative studies with lab-scale MBR and field survey were performed, in which the contributions of biodegradation and adsorption were evaluated by calculating mass balance.

In Chapter IV, the combination process of MBR and coagulation was investigated to alleviate membrane fouling. Moreover, enhanced biodegradability was evaluated by batch experiments in terms of elimination of PPCPs and applicability of coagulation-MBR was observed during long-term operation.

In Chapter V, the study on biodegradation and adsorption constant was investigated, in which target compounds were classified into each group by different kinetic models. Furthermore, the differences on removal of PPCPs between the biomass developed in MBR and CAS were studied.

In Chapter VI, the effects of microbial diversity and ammonia oxidizing bacteria on

removal of PPCPs which can be greatly achieved in MBR process were evaluated. The roles of microbial composition and the potential of cometabolic degradation were also investigated by designed batch experiments.

Model-based evaluation of PPCPs in MBR process was performed in Chapter VII, in which suitable models on based on removal pathways of each compound were suggested. Moreover, practical applicability of suggested model in predicting removal of target compounds was validated with the data of lab-scale and pilot-scale MBR.

Lastly, conclusions from this research and recommendations for further study were summarized in Chapter VIII.

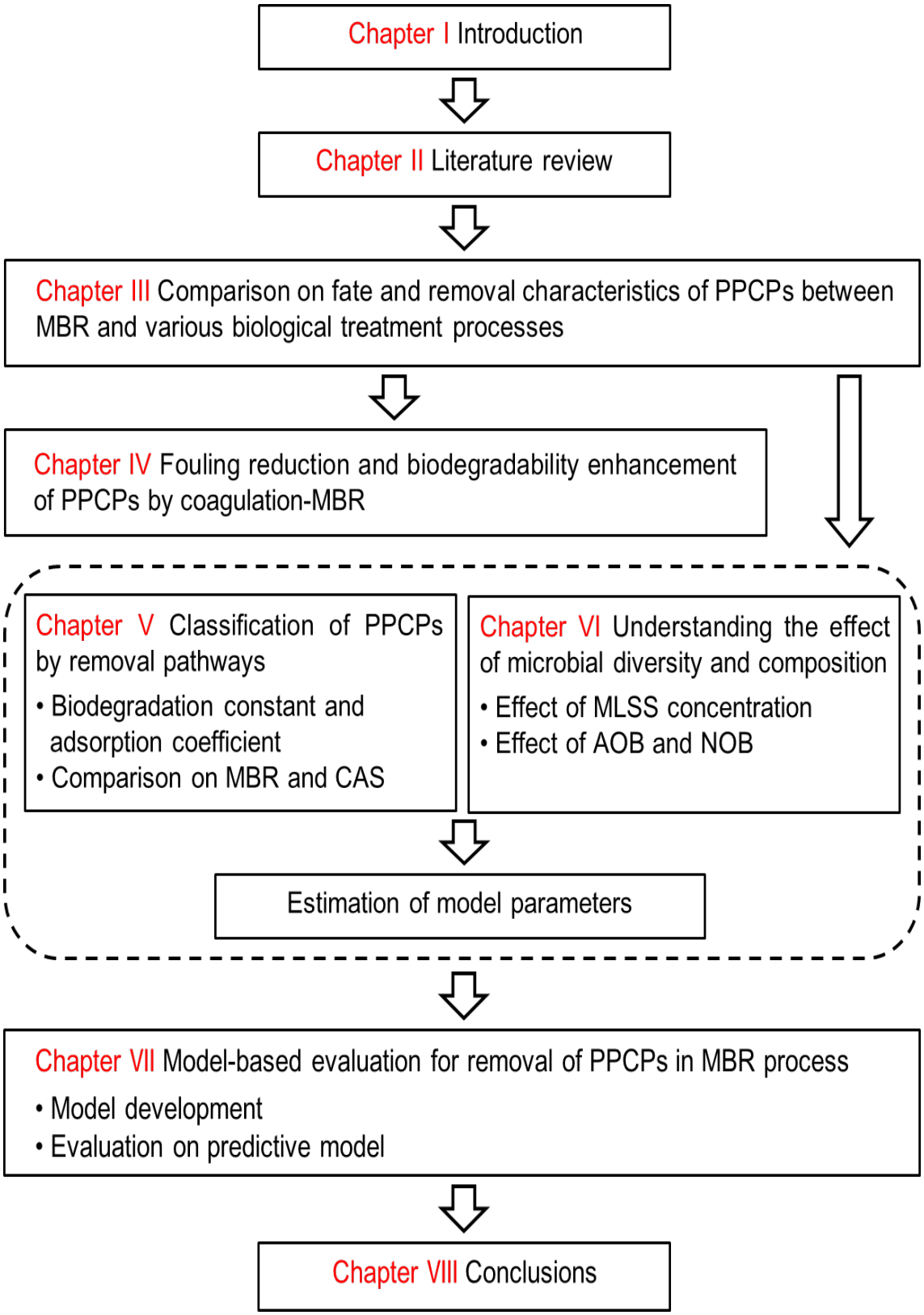

Figure 1.1 Schematic diagram of research structure

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Chapter Ⅱ

Literature Review

2.1 PPCPs

2.1.1 Classification of PPCPs

In general, PPCPs refer to any product used by individuals for personal health or cosmetic reasons or used by agribusiness to improve growth of health of livestock. These compounds are comprised of a diverse group of chemicals including, but not limited to:

◦ Prescription and over-the counter therapeutic drugs
◦ Fragrances
◦ Veterinary drugs
◦ Cosmetics
◦ Diagnostic agents
◦ Sun-screen products
◦ Nutraceuticals (e.g., vitamins)

PPCPs include a large number of chemical contaminants that can originate from human usage and excretion, veterinary applications of a variety of products, such as prescription/non-prescription medications, and fungicides and disinfectants used for industrial, domestic, agricultural and livestock practices (Daughton et al., 1999). PPCPs and their metabolites are continually introduced into the aquatic environment and are prevalent at detectable concentrations (Kolpin et al., 2002), which can affect water quality and potentially impact drinking water supplies, and ecosystem and human health (Roefer et al., 2000; Trussell., 2001; Heberer., 2002). PPCPs are frequently referred to

collectively as micropollutants or microconstituents because they are present in water at very low concentrations. These micropollutants are commonly present in waters at trace concentrations, ranging from a few ng/L to several μg/L. The low concentration and diversity of micropollutants not only complicate the associated detection and analysis procedures but also create challenges for water and wastewater treatment processes (Luo et al., 2014). Despite their low concentrations, PPCPs are more likely to reach and possibly accumulate in the aquatic environment because of their intrinsic properties such as high polarity and persistence (Sipma et al., 2010).

2.1.2 Environmental sources

PPCPs are introduced into the aquatic environments through a variety of sources including sewage treatment effluent, industrial effluent, treated sewage sludge, landfill leachate and combined sewer overflows. Sources of PPCPs are as follows (U.S.EPA, 2006):

◦ Human activity
◦ Residues from hospitals
◦ Residues from pharmaceutical manufacturing
◦ Illicit drugs
◦ Veterinary drug use, especially antibiotics and steroids
◦ Agribusiness

Especially, a large amount of PPCPs is detected in wastewater effluent via human excretion. It means that although some PPPCs are easily broken down and metabolized by the human body or degraded in the environment, others are not easily removed. Therefore, as shown in Figure 2.1 untreated PPCPs by WWTPs are the main sources and can enter domestic sewers and cause negative effect on the aquatic environment and ecosystems.

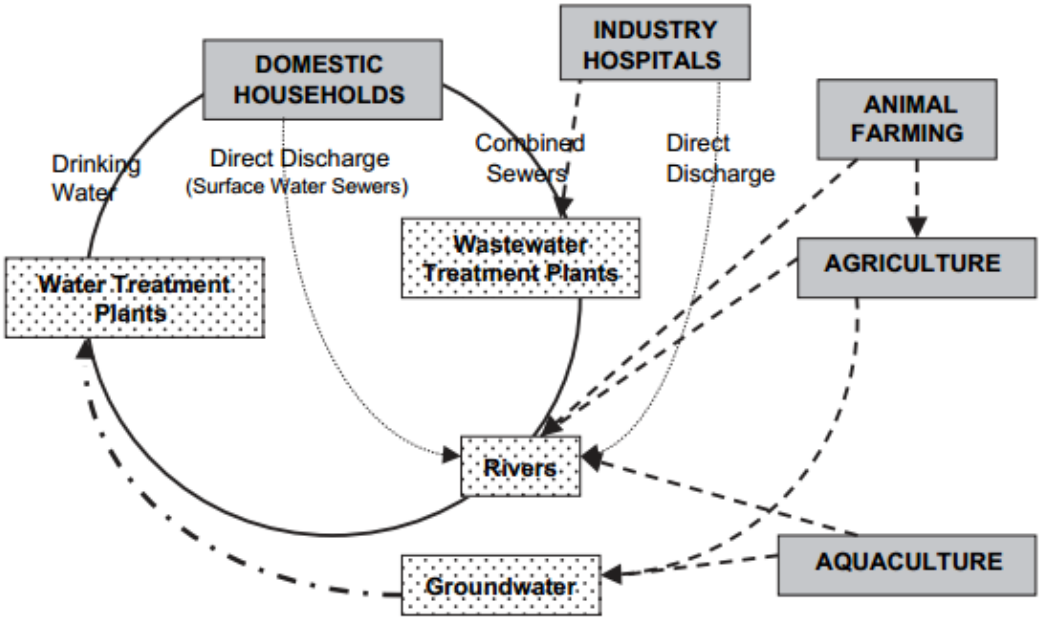

Figure 2.1 Sources of PPCPs in water environment (Petrovic et al., 2003)

2.1.3 Potential effects

The scope of human exposure to PPCPs from the environment is a complex function of many factors. These factors include the concentrations, types and distribution of pharmaceuticals in the environment; the pharmacokinetics of each drug; the structural transformation of the chemical compounds either through metabolism or natural degradation processes; and the potential bioaccumulation of the drugs (Daughton., 2008). The full effects of PPCPs mixtures of low concentrations are unknown because the amounts of these chemicals in the water supply may be in the parts per trillion or parts per billion. It is difficult to chemically determine the exact amounts present in water supplies (American Water Works Association, 2009). Many studies have therefore been focused to determining if the concentrations of these pharmaceuticals exist at or above the accepted daily intake (ADI) at which the designed biological outcomes can occur (Daughton., 2008).

Moreover, aquatic creatures are specifically vulnerable to their effects due to the high solubility of micropollutants. For instance, many studies reported that a class of antidepressants may be found in frogs and can severely impact on their development. The increased presence of estrogen and other synthetic hormones in waste water due to birth control and hormonal therapies has been linked to increased feminization of exposed fish and other aquatic organisms (Washington State University, 2009). The

chemicals within these PPCPs products could either affect the feminization or masculinization of different fishes, therefore impacting their reproductive rates (Siegrist et al., 2004). In addition to being found only in waterways, the ingredients of some PPCPs can also be found in the soil. Since some of these substances take a long time to be degraded or cannot be degraded biologically, they make their way up the food chain. Information pertaining to the transport and fate of these hormones and their metabolites in dairy waste disposal is still being investigated, yet research suggest that the land application of solid wastes is likely linked with more hormone contamination problems (Zheng et al., 2007).

2.2 Elimination of PPCPs during wastewater treatment

The removal of PPCPs in activated sludge processes includes mainly four mechanisms, i.e.: biotransformation, sorption, air-stripping, and photo-transformation (Zhang et al., 2008). The latter two mechanisms are not significantly considered in WWTPs. Air-stripping efficiency depends on the Henry coefficient of a specific compound and the aeration flow rates applied to the biological treatment. Since pharmaceuticals have Henry values smaller than 10^{-5}, whereas values larger than 10^{-3} (dimensionless air water K_H) are required to result in significant stripping at facilities employing fine air bubbling (Ternes et al., 2006). Sipma et al. (2010) reported that aeration in an MBR is typically higher, especially stripping efficiencies increase in the membrane compartment where coarse bubble aeration is applied for membrane scouring, so that for pharmaceuticals with a relative high Henry coefficient some stripping might occur. Also, photo-transformation can only take place in the conditions that water is directly exposed to sunlight. Andreozzi et al. (2003) and Matamoros et al. (2009) have suggested that some PPCPs can also be removed by photodegradation. It has been demonstrated that ketoprofen can be removed from surface and sea waters through photodegradation processes (Pereira et al., 2007; Linand et al., 2005). However, because the turbidity of wastewater is generally high they can block most sunlight and photodegradation in MBR can be negligible by high MLSS concentration and absence of secondary clarifiers. Table 2.1 shows the physico-chemical characteristics of PPCPs including molar weight, Henry coefficient, and sorption-relating coefficients. In general, biodegradation and sorption processes are considered the most important mechanisms for PPCPs, although these do not follow a general rule as their relative contribution depends on the physico-chemical properties of the compounds, the origin and composition of the wastewater and the characteristics of the wastewater treatment

facility (Cirja et al., 2008).

Table 2.1 Physico-chemical characteristics of selected PPCPs

Selected PPCPs	Molar Weight (M_w) $g.mol^{-1}$	Octanol-water partitioning Log K_{ow}	Adsorption Constant Log K_d, L/kg	Henry coefficient Air/water[-]	pK_a
Acetaminophen	151.2	0.27	3.1	2.63e-11	9.4
Antipyrine	188.2	0.38		6.65e-10	1.4
Atenolol	266.3	4.0	1.8	1.37e-18	9.6
Azithromycin	749.0	4.3	2.7	5.30e-29	8.7
Bezafibrate	361.8	4.25		8.67e-14	3.6
Caffeine	194.2	-0.07	1.5	3.58e-11	0.8
Ciprofloxacin	367.8	0.28	4.2	5.09e-19	6.2, 8.6
Clarithromycin	747.9	3.2	2.4-2.6	3.40e-01	9.0
Clofibric acid	214.6	2.84	0.7	8.96e-07	3.2
Diclofenac	294.0	4.02	2.0-2.5	4.73e-12	4.2
Diltiazem	450.9	2.7	3.2	4.72e+02	7.7
Enrofloxacin	359.4	0.7		3.40e+03	
Erythromycin	734.5	2.48	1.9	2.22e-27	8.9
Fenoprofen	242.3	3.9	3.7	1.70e+02	7.3
Ibuprofen	206.3	3.79	0.9	6.21e-06	4.9
Indomethacin	357.8	4.27	3.8	3.13e-14	4.5
Ketoprofen	254.3	3.1	1.2	2.12e-11	4.5
Levofloxacin	361.4	-0.39	3.1		5.5, 8.0
Mefenamic acid	241.3	5.1	2.6	2.57e-11	4.2
Metoprolol	267.4	1.7	1.0-1.3		9.7
Naproxen	230.3	3.2		3.39e-10	4.2
Ofloxacin	361.4	2.1			6.1
Propanolol	295.8	3.0	2.6	7.98e-13	9.4
Roxithromycin	837.1	2.8	2.3	4.97e-31	9.2
Sulfamethoxazole	253.3	0.9	1.9-2.6	6.42e-13	5.6
Triclosan	289.5	7.9	4.2	4.99e-09	7.9

This information are derived from Joss et al. (2006), Suarez et al. (2008), Narumiya et al. (2011), Snyder et al. (2007), Urase et al. (2005), Salgot et al. (2006) and Sipma et al. (2010)

2.2.1 Biodegradation

Biodegradation is the one of the major mechanisms during biological treatment. Many PPCPs were eliminated mainly by biodegradation in WWTPs despite the fact that they were designed to be persistent. Biodegradation of PPCPs can occur via different mechanisms: 1) mixed substrate growth, in which PPCPs are used as carbon and energy source and become mineralized (Vader et al., 2000); 2) co-metabolism, in which these compounds are decomposed by enzymes generated for other primary substation degradation (e.g., ammonia monooxygenase (AMO)) and are not used as carbon and energy source for microbial growth (Luo et al., 2014); and 3) single substrate growth of a small subset of specialist oligotrophic organisms, which is less common in WWTPs and more likely to occur in receiving water or sediment (Daughton et al., 1999).

The various experiments conducted in WWTPs showed removal performance of each compound and removal characteristics of each group. For instance, Alvarino et al. (2014) demonstrated that most of the organic micropollutants were readily removed under aerobic conditions (except for carbamazepine, diazepam, trimethoprim, and diclofenac, whose elimination efficiencies were below 10% in all periods), being biodegradation the main removal mechanism. The highly biodegradable compounds comprised ibuprofen, naproxen, natural estrogens (E1 and E2) and musk fragrances for which K_{bio}>5 L/g_{vss} day were obtained. Kinetic constants lower than 0.1 L/g_{vss} day were found for the previously indicated recalcitrant compounds under aerobic conditions in accordance with Plósz et al. (2012). Salgado et al. (2012) also reported that, among nonsteroidal anti-inflammatory drugs (NSAIDs), diclofenac exhibited low (< 25%) biodegradation, whereas ibuprofen and ketoprofen were biodegraded to a much higher extent (> 75%). Similar result was found by Yu et al. (2006) that in NSAIDs therapeutic class, diclofenac showed no greater than 30% removal while ibuprofen and ketoprofen both showed greater than 99% removal in the same batch study. In addition, antibiotics are generally not readily biodegradable (Verlicchi et al., 2012). They exhibit biotransformation-based removals ranging from no removal for tetracycline in a batch study (Kim et al., 2005) to 99 ± 1% for sulfamethoxazole in a pilot scale anaerobic digester (Carballa et al.,2006). Regarding polycyclic musk, Clara et al. (2011) indicated that biological degradation serves as a minor removal pathway. 15% and 30% of galaxolide and tonalide were found to be eliminated via biological transformation (Salgado et al., 2012).

Also, many researchers have reported that it is very hard to identify exactly relationships on removal between biodegradability and therapeutic class since PPCPs

within the same group have widely different chemical structures and highly variable molecular properties complicates their removal characteristics. According to Jones et al. (2005) long and highly branched side chains render a compound more persistent, whereas unsaturated aliphatic compounds are more biodegradable than saturated analogues or aromatic compounds with complicated aromatic ring structures and sulfate or halogen groups. The total removal during biological treatment generally refers to the losses of a parent compound contributed by: 1) different mechanisms of chemical and physical transformation, biodegradation and adsorption to solids (Jelic et al., 2011) and 2) the nature of each PPCPs and the operating condition of WWTPs can influence the performance of biodegradation.

2.2.2 Adsorption to sludge

Sorption of PPCPs mainly occurs via 1) absorption, in which hydrophobic interactions occur between aliphatic and aromatic groups of a compound and the lipophilic cell membrane of microorganisms as well as the fat fractions of sludge, and 2) adsorption, involving the electrostatic interactions of the positively charged groups with the negatively charged surfaces of the microorganisms and sludge (e.g., amino groups) (Ternes et al., 2004). Furthermore, absorption and adsorption are deeply related to hydrophobic interactions characterized by the Octanol-water partitioning (K_{ow}) and electrostatic interactions by the dissociation constant (pK_a), respectively. Rogers (1996) provided a general rule of thumb for applying K_{ow} to the estimation of adsorption: log K_{ow} < 2.5 indicates low adsorption potential, 2.5 < log K_{ow} < 4 indicates medium adsorption potential, and log K_{ow} > 4 indicates high adsorption potential. Compounds with a high K_{ow} value in principle have more affinity for the solid fraction, but a good correlation of the K_{ow} and adsorption coefficient (K_d, L/kg) values could not be demonstrated (Ternes et al., 2006) and they have suggested that K_d values should be experimentally determined.

For the estimation of the removal via adsorption to suspended solids and biomass solid-water distribution coefficients have been introduced, which are defined as the ratio between the concentrations of a substance in the solid and in the aqueous phase at equilibrium conditions (Carballa et al., 2005). This coefficient is commonly used to determine the fraction of PPCPs sorbed onto sludge (Eq.2.1).

$$K_{\mathrm{d}} = \frac{\mathrm{C_s}}{\mathrm{SS}\times\mathrm{C_w}} \times 10^6 \qquad \text{(Eq.2.1)}$$

Where, C_s is the adsorbed PPCPs concentration onto sludge (ng/L); C_w is the dissolved concentration of the compounds (ng/L); and SS is concentration of the mixed liquor suspended solids (mg/L).

Adsorption to sludge is a minor pathway for removal of PPCPs because of their relative low K_d value. In general, PPCPs with high log K_d value have low solubility in water and some compounds such as hormones with low log K_{ow} and K_d show weak interaction with suspended sludge. PPCPs with a K_d < 500 L/kg are eliminated by less than 10% through adsorption onto activated sludge at an average specific sludge production of 200 g m^{-3} (Ternes et al., 2006). For compounds having K_d of below 300 L/kg (log K_d < 2.48), the adsorption onto secondary sludge can be considered to be insignificant. Tadkaew et al. (2011) reported that the studied micropollutants with log D > 3.2 (e.g., estrone and nonylphenol) were easily removed (> 85%). Additionally, Verlicchi et al. (2012) indicated that adsorption onto solids is insignificant (< 5% in most cases) for most pharmaceuticals because some acidic compounds could not be adsorbed due to charge repulsion between solids and compounds. This also explains why in general removal efficiencies during primary treatment are low as has been observed amongst others (Göbel et al., 2007). In contrast, some compounds such as fragrances (galaxolide and tonalide) were found to be well removed (40%) during primary treatment (aerated grit chamber followed by circular sedimentation tank) because of their high adsorption coefficients between the solid and liquid phase, in which adsorption to suspended solids is only removal pathway (Carballa et al., 2004).

Also, nonylphenol (35% to 51%) and triclosan (11% to 41%) were detected to be moderately removed via adsorption to solids (Samaras et al., 2013). Göbel et al. (2007) and Vieno et al. (2007) reported that fluoroquinolone antibiotics, although very hydrophilic, are mainly eliminated from the aqueous phase by adsorption to sludge presumably via electrostatic interactions. Generally, the compounds that tend to be adsorbed onto solids are expected to be better eliminated by activated sludge treatment than other low-cost secondary treatment (e.g., trickling filter beds, anaerobic lagoon and constructed wet lands) (Camacho-Muñoz et al., 2012).

2.3 Elimination of PPCPs by MBR process

MBR process in wastewater treatment is currently challenging traditional methods, due to recent technical innovations and drastic cost reductions of the employed membrane (Fane et al., 2005). MBR is the combination technology of a membrane

process such as microfiltration and ultrafiltration with a suspended growth bioreactor.

The advantages of MBR as follows:

1) It can produce effluent of high quality enough to be discharged to river, surface or brackish waterways or to be reclaimed for urban irrigation.

2) It can be operated at higher MLSS concentration compared to other kinds of activated sludge systems, thus reducing the reactor volume and excess sludge production.

3) Secondary clarifiers and additional tertiary filtration are not required due to extremely low MLSS concentration in the treated effluent, thereby reducing WWTPs footprint.

4) Pathogenic bacteria and viruses are efficiently eliminated.

Therefore, many researchers have focused on application of MBR process in using water resources such as wastewater for water reclamation and sustainable management. Also, CAS process cannot efficiently deal with treatment of emerging contaminants such as PPCPs and endocrine disrupting chemicals (EDCs) that have potential effects on aquatic environment. In MBR process, however, the higher MLSS concentration by long SRT affects the overall activity of slow growing microorganisms acting in e.g., nitrification (Côté et al., 2004) or degradation of specific refractory pollutants, e.g., micropollutants (Schröder et al., 2002; Clara et al., 2004). It also affects the food to microorganisms (F/M) ratio, which is the organic matter that is available for a certain mass of microorganisms and is usually low in MBR. The relative shortage in biodegradable organic matter may force microorganisms to metabolize poorly degradable compounds. As shown in Figure 2.2 this is one explanation why removal of poorly degradable pollutants may be superior in MBR systems and why this can be achieved at lower HRT (Weiss et al., 2008). In addition, membrane acts as an effective barrier to biomass and cake layer accumulated on the membrane surface enables some extracellular enzymes to retain in the reactors, thus producing more active biological microorganisms. Sipma et al. (2010) suggested that the combination of high sludge concentrations and membrane in MBR is not only beneficial for biodegradation of PPCPs, but is also presumed to have a positive effect on the removal efficiency of PPCPs that tend to adsorb to the sludge, either due to their intrinsic hydrophobicity or via electrostatic interactions with the biomass.

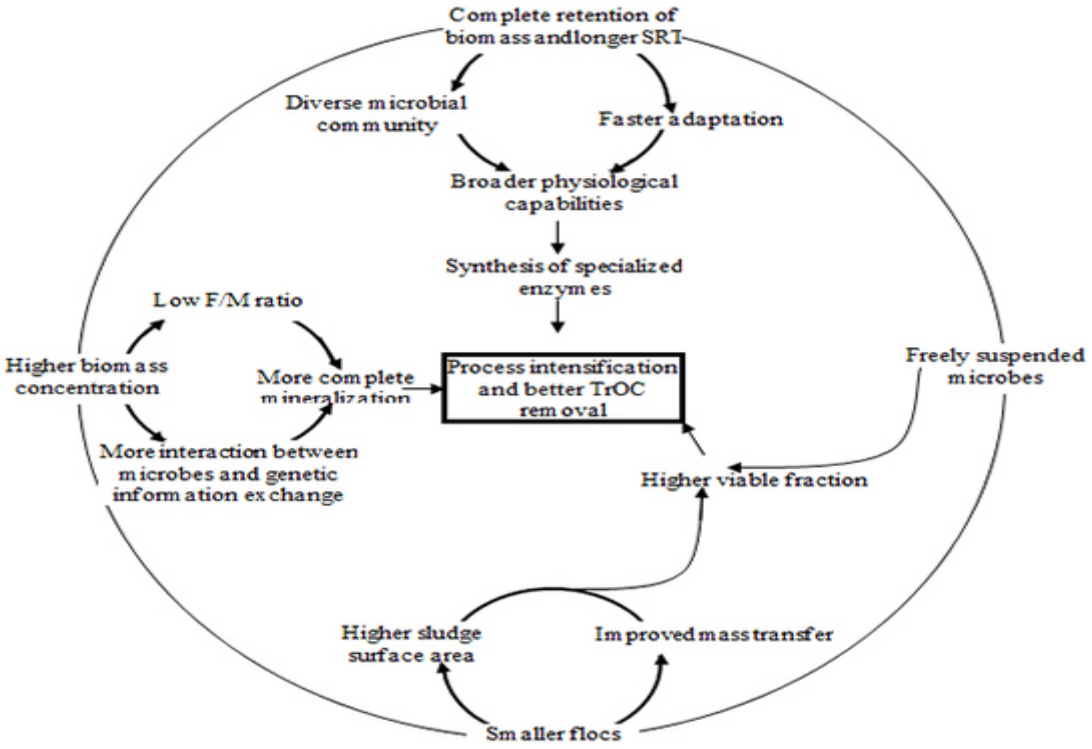

Figure 2.2 Conceptual schematic of PPCPs removal by MBR process (Hai et al., 2014)

2.3.1 Influence of operation parameters on PPCPs removal in MBR process

Whether PPCPs are removed or released from the MBR process depends on complex functions including biodegradability, adsorption to sludge characterized by hydrophobicity or electrostatic interactions and volatility. This kinetics can be partially influenced by the operation parameters, which are related to the characteristics of biomass and conditions of WWTPs (e.g., pH, redox condition and temperature). So, many researchers have concentrated on controlling the operation parameters of MBR process to achieve high adsorption potential and biodegradability.

2.3.1.1 SRT

SRT has been regarded as one of the important operating parameters that greatly affect the removal of many PPCPs. Long SRT values promote adaption of different kinds of microorganisms and the presence of slower growing species which could have a greater capacity for removing more recalcitrant compounds while simultaneously improving suspended solids separation (Kreuzinger et al., 2004). Strenn et al. (2004)

found a clear dependence of the removal rates on the SRT was observed for ibuprofen and bezafibrate. The positive effect of long SRT was also reported by Lesjean et al. (2005), who found that the removal of PPCPs increased with a sludge age of 26 days and inversely decreased when the sludge age was set at 8 days. According to Wick et al. (2009) the activated sludge treatment with an elevated SRT of 18 days could achieve considerably higher removal of beta blockers and psycho-activate drugs in comparison with the same treatment with shorter SRT of 0.5 day. Clara et al. (2005) also suggested that the SRT allowing nitrogen removal (nitrification and denitrification) above 10 days can enhance the elimination of some biodegradable compounds (e.g., ibuprofen, bezafibrate, natural estrogens and bisphenol A). Removal efficiencies of target compounds observed at different sludge ages, it emerges that SRT equal to 20-25 day promotes the removal of atenolol and clarithromycin, slightly higher values (around 30 day) enhance diclofenac and erythromycin removal and around 50 d a larger number of compounds are better removed (e.g., naproxen, lidocaine, ciprofloxacin, sulfamethoxazole and cyclophosphamide) (Verlicchi et al., 2015).

Although, SRT has been represented as determinative for removal of PPCPs, better removal performance is always not achieved at the condition of long SRT. For instance, Joss et al. (2005) suggested that variation of the sludge age between 10 and 60–80 days showed no noticeable effects on removal efficiency of the investigated pharmaceuticals. High SRT (20 days) also seemed not to appreciably affect the biodegradation of bisphenol A (Stasinakis et al., 2010).

2.3.1.2 HRT

Removal efficiency of PPCPs in MBR process could be related to the HRT because it determines the contact time between the pollutant and the microorganisms, which allows for biodegradation and sorption. The micropollutants having slow and intermediate kinetics such as fluoxetine or some antibiotics will experience less effective biodegradation at shorter HRT or increasing loading rates (Fernandez-Fontaina et al., 2012). Huang et al. (2008) suggested that HRT in the range from 5 to 14 h achieved minor removal of diethylhexyl-phthalate (DEHP), while higher HRT increased DEHP accumulation in the system and DEHP retention in the waste sludge.

However, some studies have been reported that removal efficiency of PPCPs is not affected by HRT. Göbel et al. (2007) found that removal performance was similar between CAS operated with HRT of 31 h and a fixed bed reactor operated with HRT as low as 1 h, which was ascribed to a higher bioactivity of the sludge per reactor volume.

A direct influence of the HRT on biodegradation of PPCPs does not become clear from the literature, an increased contact time between PPCPs and biomass has been suggested as the reason for an improved biodegradation of several acidic PPCPs at a decreased pH (Urase et al., 2005). Due to the decoupling of HRT and SRT in MBR, most MBR researches have reported no obvious effect of HRT under the tested ranges (Hai et al., 2015). For instance, no obvious influence of HRT (3.9-8 h) on bisphenol A removal was observed in an MBR (Chen et al, 2008). Reemtsma et al. (2008) reported a statistically insignificant effect of HRT (7–14 h) on the removal of a range of polar PPCPs including those which are easily degradable and those which are highly persistent. Bernhard et al. (2006) revealed that the reduction of the HRT from 10 to 7 h did not influence the removal of selected non-adsorbing, persistent PPCPs in a lab-scale MBR.

2.3.1.3 Characteristics of sludge

Characteristic of sludge is the important factors for biodegradation and varies on depending on wastewater treatment processes. Some enzymatic activities increase proportionally to the higher specific surface area of MLSS, which is directly related to the floc-structure. The activated sludge composition varies both with the influent composition and operating conditions adapted to the wastewater treatment system (Chang et al., 2003). Comparing the MBR and CAS systems, Cicek et al. (1999) showed that the biomass in the MBR has higher viable fraction than in the CAS. This phenomenon can be attributed to improved mass-transfer conditions in the MBR favored by smaller flocs and the presence of many free-living bacteria.

Shariati et al. (2011) reported that the removal of acetaminophen and paracetamol was observed from 20 to 40% when the MLSS concentration was operated from 2 to 15 g/L. Because acetaminophen is a hydrophilic compound, the improvement of removal performance could be attributed to the increase of biodegradation. Li et al. (2011) summarized that the removal rate of carbamazepine did not increase much beyond MLSS concentration of 5 g/L. This indicated that due to the insignificant adsorption of carbamazepine onto MLSS, biodegradation, in contrast to adsorption, played the main role in carbamazepine removal by the MBR. Whereas, under the MLSS concentration of approximately 1 g/L the removal rate of carbamazepine was the lowest. This underscored the importance of maintenance of an adequate amount of biomass in the reactor to achieve satisfactory degree of recalcitrant pollutant degradation.

2.3.1.4 Redox condition

Redox conditions may cause the observed differences by having an effect on certain wastewater or sludge characteristics as well as on the biodiversity of the microbial flora present (Göbel et al., 2007). Studies on relationships between redox conditions and removal of PPCPs in MBR have not been investigated very much. The reported results revealed mostly insignificant difference between aerobic and anoxic MBRs in terms of PPCPs removal. For example, some researchers reported that negligible level of removal of carbamazepine using different configurations of MBR (sequential anoxic–aerobic MBR and aerobic MBR) (Clara et al., 2005; Abegglen et al., 2009). Some persistent substances such as diclofenac, sulfamethoxazole, trimethoprim and carbamazepine showed minor removals (< 25%) by the biological treatment with either nitrifying (oxic) or denitrifying bacteria (anoxic) (Suárez et al., 2010).

On the other hand, there are some studies, which have highlighted better removal under anoxic environment, either in MBR or in batch tests. Hai et al. (2011) reported carbamazepine (a persistent trace organic) to be degraded only under anoxic environment in their batch tests. In MBR treatment, the removal of carbamazepine was found to be 68% and less than 20% under anoxic and aerobic conditions, respectively. Zwiener et al. (2003) also showed that diclofenac was not degraded in short-term biodegradation tests under aerobic conditions, whereas it was degraded under anoxic conditions. Better removal of diuron during batch tests under anoxic environment (> 95%) in comparison to that in aerobic condition (60%) (Stasinakis et al., 2009). Goel et al. (2003) focused on the effects of redox conditions in aeration tank, showing the different results. The study reported that removal of the nonylphenol ethoxylate surfactant was higher in the oxic reactors (50 to 70%) compared to the anoxic reactors (30 to 50%). Similarly, DEHP were removed by 15%, 19% and 62% in anaerobic, anoxic and aerobic reactors (Huang et al., 2008).

2.3.1.5 pH

Removal performance of PPCPs may be affected by pH variation during wastewater treatment process. The acidity or alkalinity of an aqueous environment can vary the elimination of micropollutants from wastewater by influencing both the physiology of microorganisms (pH optima of microbial enzyme activities) and the solubility of micropollutants present in wastewater (Cirja et al., 2008). Urase et al. (2005) found that higher removals were observed in the period of lower pH operation. More than 90% and

70% removal of ibuprofen and ketoprofen were respectively obtained when pH in the reactor was below 6 and 5. While the removal of neutral compounds such as 17α-ethinylestradiol, carbamazepine, propyphenazone, and benzophenone was not significantly influenced by pH, the removal of some compounds such as clofibric acid, gemfibrozil, fenoprofen, naproxen, diclofenac and indomethacin in MBR process was obviously affected by pH and higher removal was observed at lower pH (pH = 4.3 - 5). Similarly, Tadkaew et al. (2010) investigated the removal of ionisable and non-ionisable trace organics by MBR treatment using different mixed liquor pH ranging from 5 to 9. High removal efficiency of the ionisable compounds was observed at pH 5 while removal efficiency of two non-ionisable (bisphenol A and carbamazepine) compounds was independent of the mixed liquor pH.

There are some practical constraints against operation under acidic pH in spite of the possibility of improved adsorption of certain ionisable PPCPs on sludge. For example, acidic pH may have adverse impact on certain microbial groups, which may in turn lead to reduction of total organic carbon (TOC), total nitrogen (TN), and total phosphorous (TP) removal (Zhang et al., 2005; Baldwin et al., 2001). Cirja et al. (2008) demonstrated that the hydrophobicity of norfloxacin varies with pH, with the hydrophobicity being very low at pH < 4 and pH > 10 and the maximal hydrophobicity was reached at a pH of 7.5. It was also reported that biodegradation of clofibric acid was impaired at low pH operation, and improved removal occurred only after a lag phase following the return of the mixed liquor pH to neutral (Bo et al., 2009).

2.3.1.6 Temperature

Temperature could contribute to promote biological activity, resulting in the efficient removal of micropollutants by biodegradation and sorption to sludge. At warmer temperature, higher removal performance can be achieved because of promoted microbial activities (Nie et al., 2012; Qiang et al., 2013). Vieno et al. (2005) found that the total concentration of all the studied PPCPs in the effluent water was 3-5 times higher in winter time (about 2500 ng/L) than during the other seasons (about 500-900 ng /L). Hai et al. (2011) provided unique insight into the effect of dynamic short term temperature variation on PPCPs removal by MBR treatment. With a few exceptions, operation at 45 ℃ clearly excreted detrimental effects on the removal efficiency of the PPCPs selected in that study. The removal of most hydrophobic compounds (log D > 3.2) was stable during operation under a temperature range of 10-35 ℃. On the other hand, for the less hydrophobic compounds (log D < 3.2) a comparatively more

pronounced variation between removals in the lower temperature ranges was observed.

In addition to temperature, other factors like overall pollutant loading, biomass characteristics, and WWTPs-relating parameters such as redox conditions or pH of mixed liquor can impact on the seasonal variations in PPCPs removal. Accordingly, investigation on the effect of temperature under the identical conditions with experimental design should be carried out.

2.3.2 Comparison of PPCPs removal in MBR and CAS process

Although many studies have been conducted comparing the removal performance of PPCPs during the treatment of MBR and CAS, there have been several conflicting reports on whether MBR can have efficient removal of PPCPs compared to that eliminated by CAS. Table 2.2 listed the comparison of removal efficiency between CAS and MBR process, as well as includes removal performance of results on our lab-scale study, for which average performance, with maximum and minimum percentage is represented.

PPCPs removal efficiency has been observed to be very similar, and high for both treatments (e.g., for ibuprofen, naproxen, acetaminophen and paroxetine) (Cirja et al., 2008; Oulton et al, 2010), while some compounds such as the anti-epileptic drug carbamazepine and diuretic hydrochlorothiazide can pass through both the systems (Radjenovic et al., 2007; Radjenovic et al., 2009). Oppenheimer et al. (2007) reported no significant difference in removal efficiencies of ibuprofen, triclosan and caffeine by both CAS and MBR process. Kimura et al. (2005) indicated that PPCPs can be grouped into three categories based on the degree of their removal: 1) easily removed by both CAS and MBR (e.g., ibuprofen), 2) not efficiently removed by either of them (e.g., carbamazepine, clofibric acid, dichloprop, and diclofenac) and 3) better removed by MBR (e.g., ketoprofen, mefenamic acid, and naproxen).

In contrast, Bernhard et al. (2006) suggested that treatment by MBR resulted in significantly better removals compared to CAS for poorly biodegradable compounds such as diclofenac, mecoprop, and sulfophenyl carboxylates which was attributed to the long SRT in MBR. Reif et al. (2008) observed a significant removal of ibuprofen (98%), naproxen (84%) and erythromycin (91%) by a pilot-scale MBR. The author also reported a moderate removal (>50%) of sulfamethoxazole and musk fragrances (i.e., galaxolide, tonalide, and celestolide). Verlicchi et al. (2012) highlighted that in the MBR, compared with CAS, effect of higher MLSS concentration, development of different bacterial species within biomass, and smaller sludge flocks that may enhance adsorption on the

surface of different compounds greatly contributes to the removal of PPCPs from the stream.

In some reviews, average removal eliminations of PPCPs, in which removal efficiency of some compounds like carbamazepine and propyphenazone in effluent was frequently higher than influent levels. It means that they were not removed by membrane filtration and biological treatment. For carbamazepine, the elevated effluent concentrations are most likely due to enzymatic cleavage of the glucuronic conjugate of carbamazepine and release of the parent compound in the treatment plant (Vieno et al., 2007). As shown in removal of some macrolides negative elimination can be explained by the presence of input conjugate compounds that are transformed into the original compounds during treatment, but no firm conclusion can be made about their biotransformation because these conjugates were not included in the analysis (Radjenovic et al., 2007). Since they are mainly excreted with bile and feces, they could be enclosed in feces particles and released during biological treatment, suggesting that the pharmaceutical load is underestimated when based exclusively on the dissolved fraction and the fraction adsorbed to the suspended solids (Göbel et al., 2007).

Table 2.2 Comparison of removal efficiency between CAS, MBR (other literatures) and MBR (this study)

PPCPs	CAS					MBR					MBR (this study)			
	Avg. (%)	SD (±)	Min. (%)	Max. (%)	Ref.	Avg. (%)	SD (±)	Min. (%)	Max. (%)	Ref.	Avg. (%)	SD (±)	Min. (%)	Max. (%)
Sulpiride											3	18	-29	33
Atenolol	45	30	5	97	2,3,8,9,11,13,30,31	81	10	66	96	2,3,6,24,32	59	17	36	87
Acetaminophen	100	0	98	100	1,2,3,4,5	100	0	97	100	2,3,6,7	95	11	72	100
Theophylline	95	3	90	98	38	100	1	98	100	38	94	4	86	98
Sulfapyridine											19	33	-31	67
Caffeine	95		50	100	8,10,11,21,36	99		53	100	6,22,23,33	96	6	80	100
Trimethoprim	15	28	-40	82	3,8,9,10,11,13,26,35,36	70	12	-2	90	3,6,23,26	36	25	5	70
Lincomycin											90	9	72	100
Levofloxacin	55	10	43	48	38	53	24	38	64	38	82	8	70	92
Norfloxacin	78	27	59	95	38	83	22	60	90	6,38				
Tetracycline											87	7	76	95
Ciprofloxacin	77	9	62	82	38	79	13	63	89	6,38	87	6	76	95
Oxytetracycline														
Sulfamethoxazole	38	51	4	99	2,3,8,9,10,11,12,17,26,27, 35,39	92	1	52	95	2,3,6,12,22,23,26,27,39	55	31	-10	87
Metoprolol	44	32	3	77	2,3,8,9,11,13,30,31	48	16	36	59	2,3,6				
Azithromycin	-22	70	-68	38	38	65	30	65	78	6,38	67	21	25	95
Propranolol	15	55	-60	40	3,38	72	6	65	78	3	29	0	-57	81
Furosemide						89	14	75	97	6,38	69	23	33	94
Diltiazem											58	19	31	89
Carbamazepine	0	32	-122	62	2,3,8,9,10,11,12,13,14,19,21, 27,30,35,36	13	4	-22	28	2,3,6,7,12,13,27,33,34	-17	21	-40	23
DEET			5	80	10,35			0	78	23,33,34	53	33	-3	100
Clofibric_acid	25	16	0	94	2,8,9,10,11,15,18,28,29	67	20	41	72	2,15				
Ketoprofen	50	18	11	100	1,2,3,8,9,11,15,16,18,19,20, 21	72	23	44	97	2,3,22,23,24	87	10	70	99
Clarithromycin	20	18	9	21	38	63	21	-34	80	6,38,39	50	20	12	77
Naproxen	56	20	-2	99	1,2,3,8,9,11,12,13,14,15,16, 17,18,19,20,21	88	10	36	100	2,3,6,12,22,23,24,25	97	3	89	100
Roxithromycin	25	26	-20	66	12,26,27	70	15	33	86	12,27,38,39	51	15	29	66
Crotamiton											24	12	7	45
Bezafibrate	70	20	9	99	2,3,8,9,10,11,13,27	90	8	76	97	2,3,13,27	93	7	79	99
Fenoprofen														
Diclofenac	21	31	-143	81	1,2,3,4,8,9,10,11,12,13,14,16	34	25	-8	87	2,3,7,12,13,22,23,24	36	26	7	90
Indometacin	15	32	-41	63	2,3,16	43	3	40	47	2,3				
Triclosan			61	99	8,10,11,37	92		46	99	6,7,23,33	94	-	94	94
Mefenamic_acid	31	18	0	70	2,3,8,9,11,15	63	21	36	89	2,3,15	60	40	-40	90
Triclocarban						95	2	92	98	6,23,33	95	8	81	99

Avg.: average removal efficiency, SD: standard deviation, Min.: minimum percentage, Max.: maximum percentage and Ref.: references

Ref.: 1. Yu et al. (2006), 2. Radjenovic et al. (2007), 3. Radjenovic et al. (2009), 4. Gomez et al. (2007), 5. Levine et al. (2006), 6. Kim et al. (2014), 7. Cartagena et al. (2013), 8. Behera et al. (2011), 9. Kasprzyk-Hordern et al. (2009), 10. Loos et al. (2013), 11. Santos et al. (2009), 12. Joss et al. (2005), 13. Paxéus. (2004), 14. Suarez et al.(2005), 15. Kimura et al. (2005), 16. Lishman et al. (2006), 17. Carballa et al. (2005), 18. Kosjek et al. (2007), 19. Nakada et al. (2006), 20. Santos et al. (2007), 21. Singer et al. (2010), 22. Tadkaew et al. (2011), 23. Kim et al. (2007), 24. Quintana et al. (2005), 25. Urase et al. (2005), 26. Göbel et al. (2007), 27. Kreuzinger et al. (2004), 28. Zwiener et al. (2003), 29. Heberer et al. (2002), 30. Vieno et al. (2007), 31. Alder et al. (2010), 32. Reif et al. (2008), 33. Snyder et al. (2007), 34. Bernhard et al. (2006), 35. Terzić et al. (2008), 36. Zhou et al. (2010), 37. Pothitou et al. (2008), 38. Kazama. (2014) and 39. Sahar et al. (2011).

2.4 Elimination of PPCPs by coagulation

Coagulants react with the suspended and colloidal particles in the water, causing them to bind together and thus allowing for their removal in the subsequent treatment processes (Lia et al., 2006). The aggregation mechanisms through which particles and colloids are removed include a combination of charge neutralization, entrapment, adsorption and complexation with coagulant ions into insoluble masses (Duan et al., 2003; Matilainen et al., 2010; Verma et al., 2012).

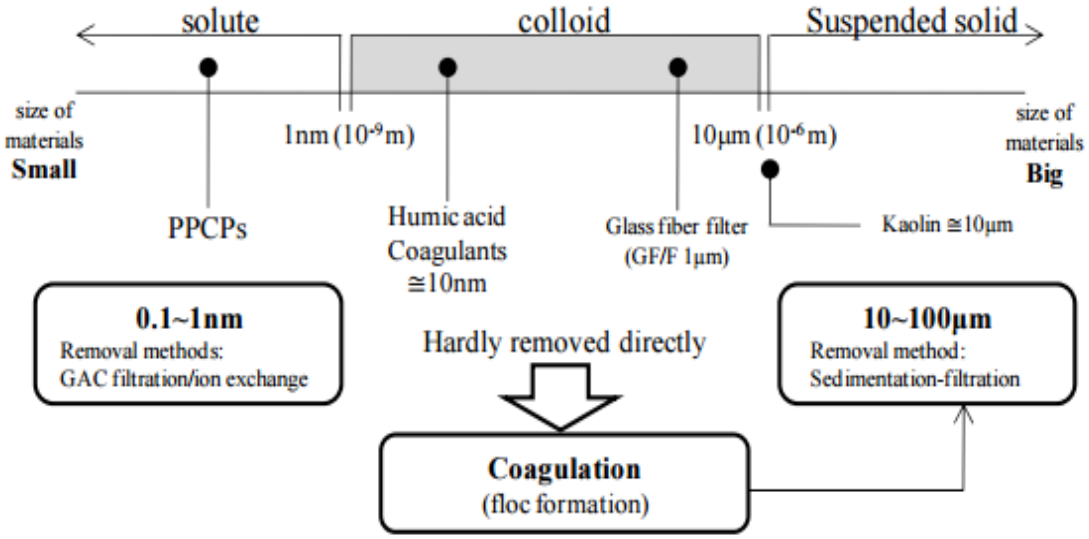

Figure 2.3 The size of pollutants in raw water and efficient removal processes

Also, the coagulation is usually applied for removal of phosphorus as post treatment of biological reactor in WWTPs. Especially, the concentration of phosphorus is not removed efficiently in A/O (anoxic/oxic) MBR due to the absence of anaerobic tank, in which release of phosphorous from stored polyphosphates is generated. Discharge of phosphorous above water quality standard in water environment leads to eutrophication problems. Though coagulation, in combination with the other physicochemical water treatment processes of flocculation and sedimentation, has been found to be effective for removal of bulk natural organic matter (NOM) and phosphorus from wastewater, previous studies have been reported that elimination of PPCPs is not significant (Choi et al., 2006; Dempsey et al., 1984; Le-Minh et al., 2010; Ternes et al., 2002; Huerta-Fontela et al., 2011; Kim et al., 2007; Snoeyink et al., 1985; Vieno et al., 2007).

As shown in Figure 2.3 efficient removal of PPCPs cannot be achieved just by coagulation. Thus, application on combination of coagulation and biological treatments might help in eliminating PPCPs. For instance, removal of diclofenac has been reported to be inefficient by MBR, while some of the hydrophobic compounds, such as hormones, which are reported to be significantly removed by MBR treatment, were poorly removed by coagulation treatment. Given the complementary nature of these processes, it is likely that simultaneous addition of coagulant into MBR may improve the removal of trace organic contaminants (Hai et al, 2015).

2.4.1 Description of coagulants used in this study

2.4.1.1 PAC

PAC is a blend of chemicals that can achieve the same or better coagulant results as alum and increasingly preferred for wastewater treatment. The cost of the PAC is lower than the other conventional coagulants such as alum, soda ash, and lime. Against the conventional coagulants its distinct advantages are as follows:

◦ Lower dose requirement
◦ Pre-neutralized characteristic (no requirement for any neutralizing agent)
◦ Shorter flocculation time
◦ Reduced number of backwashing frequency
◦ Higher quality of the treated water.

However, in general, PAC produces a large amount of sludge including aluminium residues, which contains mixture of organic and inorganic materials and hydroxide precipitates. On the contrast, among a number of alternative coagulants including aluminium-based additives, PAC have been widely used for wastewater applications due to representative property, their basicity, which is the ratio of hydroxyl to aluminium ions in the hydrated complex and in general the higher the basicity, the lower will be the consumption of alkalinity in the treatment process and hence impact on pH (Gebbie., 2001).

2.4.1.2 Chitosan

Recently, there has been considerable attention in the development and application of

natural coagulants. In the wastewater field, significant cost reduction from effective use of chemicals and sludge control can be achieved. There are many kinds of natural polymer coagulants such as starch, chitosan, lignin, protein and algae (Renault et al., 2009; Shareef., 2009; Zeng et al., 2013). Among these coagulants, advantages of chitosan are as follows:

◦ Inexpensive and biodegradable
◦ Nontoxic material for mammals
◦ Binding toxic heavy metals or non-degradable compounds
◦ Different physicochemical characteristics

Moreover, chitosan is found to be more effective than other polymers like synthetic resins, activated charcoal, and even chitin itself, since its molecular structure is liner type and the amino group in acid solutions is an effective functional group that can be altered chemically for production of other derivatives with specific useful characteristics as effective absorptive agents (No., 2000).

2.4.2 Factors governing removal performance

The effectiveness of coagulation is affected by several factors including coagulant type and dosage, mixing speed, pH, alkalinity, temperature as well as the presence of divalent cations and concentrations of destabilizing anions (biocarbonate, chloride, sulphate, etc.) (Duan et al., 2003; Matilainen et al., 2010; Verma et al., 2012). Therefore, improvement of MBR performance and efficient removal of PPCPs can be accomplished under the optimal conditions.

2.4.2.1 Type of coagulants and dosage

Few studies have been reported to the effect of coagulant types for PPCPs removal. Because inorganic coagulants are cost effective compared to organic coagulants they are commonly used in coagulation process (e.g., aluminium sulphate, ferric chloride and polyaluminium chloride (PAC), etc.). Firstly, the use of aluminium sulphate as a coagulant was proven to be highly effective in removing certain hydrophobic PPCPs, namely chlordiazepoxide, zolpidem, bromazepam, clopidogrel, doxazosin, warfarin, and betaxolol (Huerta-Fontela et al., 2011). Aluminium sulfate and ferric chloride or chemical lime softening removed some polyaromatic hydrocarbons (PAHs) but removed

< 25% of most other EDC and PPCPs (Westerhoff et al., 2005). Carballa et al. (2005) reported that in the case of musk pharmaceuticals, ferric chloride or aluminium sulfate leaded to similar eliminations (around 50%) and the elimination of diclofenac was higher with both coagulants (around 70%).

Ferric chloride could not remove several pharmaceuticals in surface waters (diclofenac, carbamazepine and bezafibrate) and pesticides were poorly removed by coagulation (Meszaros et al., 2013). According to Suarez et al. (2009) the removal of three musk compounds, namely tonalide, galaxolide, and celestolide, from hospital wastewater were significantly eliminated at the dosage of 25 mg/L. The removal efficiency of these compounds does not seem to be improved greatly by high dosages of coagulant, as another study has shown that 250 mg/L added to an urban sewage treatment plant indicated similar removal efficiencies (Carballa et al., 2005). Moreover, Westerhoff et al. (2007) demonstrated that the elimination by coagulation for PPCPs and EDC removal was ineffective and, among detected 61 PPCPs and EDC, most compounds were removed by less than 15% except for the compounds which consist of aromatic ring (high removal of more than 85%). Especially, since acidic compounds remain partially ionized in aqueous phase, comparatively higher coagulant dosage may be required for their removal. For example, Zorita et al. (2009) achieved less than 25% removal of diclofenac by applying a ferric chloride dose of 70 mg/L as a tertiary treatment of sewage wastewater, while in another study Carballa et al. (2005) reported 70% removal applying a higher dose of 250 mg/L.

PAC is synthetic polymer dissolved in water and by applying PAC as coagulants suspended micropollutants in wastewater which are precipitated with the PAC and can be partially removed. For instance, PAC had a higher removal performance than ferric chloride in the removal of estrogen compounds using dosages of 5.4 mg/L and 12.2 mg/L, respectively, however removal efficiencies were not found to be greater than 40% for any of the estrogens tested (Bodzek et al., 2006). Choi et al. (2008) also utilized PAC, with the best removal efficiencies in this study observed at a dosage of 40 mg/L, with reported removal efficiencies of above 50% for four of the seven antibiotics tested. In the study by Carballa et al. (2005) some compounds such as diclofenac, galaxolide and tonalide were efficiently eliminated by PAC dosage, but removal performance of naproxen and diapezam was less than 10%. Chen et al. (2010) interestingly noted the superiority of polyaluminium ferric chloride (PAFC) over PAC for decolouration of petrochemical wastewater. The superior performance of PAFC is caused by the combination of unique advantages of both aluminium and iron salts, thus, allowing bulky flocs to form and settle rapidly.

Although the use of natural coagulants such as polysaccharides and chitosan to eliminate trace organic contaminant have not yet been demonstrated, they are biodegradable, non-toxic and environmental friendly, and can be efficient technology by applying them to MBR process. However, systematic studies on comparison between the trace organic contaminant removal performance of various pre-hydrolyzed (i.e., organic coagulants) and hydrolyzable (i.e., inorganic coagulants) coagulants could not be identified in the literature (Alexander et al., 2012). Accordingly, the research on development of new composite coagulants of inorganic coagulants and organic coagulants for removal of PPCPs in wastewater treatment should be investigated. Also, hybrid process combining composite coagulants and biological treatments like MBR may provide useful information and insights.

2.4.2.2 Effect of pH and temperature

As the removal of PPCPs can be influenced by coagulant types, variation of pH can have impact on the effectiveness of coagulation by change of charge and physicochemical characteristics. The media pH influences the extent of dissociation of the trace organic contaminants, and can, thereby, result in compound-specific removal performance during application of a certain type of coagulant (Alexander et al., 2012). The optimal pH range for coagulation is 6 to 7 when using aluminium-based coagulants and 5.5 to 6.5 when using iron-based coagulants. Vieno et al. (2006) demonstrated moderate removal of the PPCPs such as ibuprofen, diclofenac and bezafibrate by using a ferric sulphate coagulant at the pH 4.5. Also, PAC coagulants are pre-neutralized, have insignificant effect on the pH of water and therefore decrease the need of such pH correction. Excessive amounts of coagulant may be needed to lower the pH in order to control the optimal range of pH in high alkalinity water. In these cases, it may be advantageous to use acid in addition to the coagulant to decrease the amount of coagulants needed and effectively lower chemical costs. On the other hand, some researchers have reported that detected compounds may represent negligible removal performance by coagulation over a wide range of pH. For instance, although Chang et al. (2004) observed a significant effect of pH on total organic carbon removal, no obvious change in EDC removal was observed for coagulation under different pH conditions (from pH 5 to 11.4).

Temperature also affects the coagulation process, allowing viscosity of wastewater to change. Thus lower temperature of WWTPs can reduce the hydrolysis and precipitation kinetics. However, PAC can be beneficial over the traditional coagulants like iron-based

and aluminium-based coagulants in low temperature conditions because these coagulants are already hydrolyzed, and therefore temperature tends to have less impact on the coagulation process. Carballa et al. (2003) investigated the removal performance of various coagulants (e.g., aluminium sulfate, ferric chloride and PAC) under two different temperatures (12°C and 25°C). In this research, neutral compounds such as galaxolide and tonalide were significantly eliminated at two different temperatures, while among acidic compounds only diclofenac was affected at 25°C.

2.4.3 Combination of MBR and coagulation for PPCPs removal

In order to resolve drawbacks of MBR technology, in which though elimination of PPCPs is superior to the CAS system, efficient removal is not achieved, recently, many researchers have focused on MBR-hybrid processes including nanofiltration (NF) or reverse osmosis (RO) that can prevent micropollutants having smaller size from passing through the membrane barrier and AOP process using ozone, fenton, ferrate (Ⅵ) and UV irradiation. Specifically, application of AOP can be more efficient in the conditions of MBR than other kinds of treatment processes due to the absence of suspended solids in effluent that can scatter the UV irradiation and reduce oxidation process.

Among many kinds of advanced treatments applied in both field and lab scale treatment, combination of MBR and coagulation can be one of the alternatives to enhance removal performance of PPCPs. The sorption mechanism of coagulation, combined with the biodegradation of MBR, may be beneficial in terms of helping to mitigate the problems of membrane fouling (Hai et al., 2011; Le-Clech et al., 2006) and improving the removal efficiency of trace organic contaminants (Leiknes, 2009). Similarly, Zaisheng et al. (2009) reported that the combination of MBR and coagulation has been found to be effective in the treatment of textile dyeing wastewater. It has also been shown to be effective in removing certain trace organic contaminants (Serrano et al., 2010).

In general, MBR process with coagulation for elimination of PPCPs can be described by mainly two types: 1) MBR with pre/post coagulation and 2) direct injection into MBR process. The former type is used as the main purpose of phosphorous removal because conventional phosphorus removal processes using biological treatments cannot meet the discharge regulatory requirements that strictly have been limited to preserve surface water quality. The application of chemical coagulation/flocculation using coagulants such as alum, ferric chloride and PAC as pre or post treatment with MBR has been used for treatment of industrial wastewater such as dairy or piggery effluents (Chen et al.,

2012; Kornboonraksa et al., 2009). Coagulants, when directly added to MBR, have been found to reduce membrane fouling, possibly due to modification of the particle size distribution of the mixed liquor suspended solids and to improve removal performance of PPCPs. Various investigations have been studied for flux increase by control of transmembrane pressure (TMP) and fouling mechanisms by adding coagulants directly into MBR. However, there have been only a few studies on removal performance and elimination characteristics of PPCPs in the combination of MBR with coagulation. For instance, Zou et al. (2007) reported that when $Fe(OH)_3$ was injected to an MBR removal performance of dye wastewater and reduction of membrane fouling were accomplished. Even at a 25% higher volumetric loading rate, the coagulant-amended MBR achieved about 10 % higher dye removal than a conventional MBR.

2.5 Model development based on biodegradation

Various models have been proposed in the literature by many authors to deal with removal of PPCPs in WWTPs. These studies for developing models have always targeted either the biological treatment processes which are mainly operated by activated sludge system as well as the various aspects of engineering for cost-effective operation and energy savings. Indeed, such a tool is very beneficial in understanding the removal mechanisms of target compounds and predicting their emission into environment for sustainable water management. As activated sludge processes have been well established and largely applied in the field of wastewater treatment by the development of activated sludge Model (ASM), it is very important to better understand removal pathways of PPCPs in WWTPs, with particularly biomass in biological treatment like CAS or MBR systems.

As described in chapter 2.2, removal of PPCPs within activated sludge systems can be primarily achieved through biodegradation and adsorption based on elimination of dissolved or solid compartment and equilibrium mechanisms, respectively, so that several studies have focused on their removal characteristics and mechanisms (Figure 2.4). In previous studies modeling of emerging contaminants including hormones and pharmaceuticals was proposed (Urase et al., 2005; Plosz et al., 2010). By Joss et al. (2006), a simple classification scheme was suggested to characterize the biological degradation of pharmaceuticals, musk fragrances and estrogens during wastewater treatment. Also, Fernandez-Fontaina et al. (2013) reported biodegradation and sorption kinetic constants in MBR process to elucidate the capability of biomass. In addition to

biodegradation and adsorption, influence of volatilization on removal of PPCPs was evaluated by Byrns et al. (2001), who studied target compounds with a large range of physicochemical characteristics, suggested that volatilization was not greatly affected on the removal of PAHs or pesticides. Pomiès et al. (2013) summarized the reviews of modeling, in which volatilization concerns only volatile micropollutants, but the limit of volatility is rarely and not clearly mentioned.

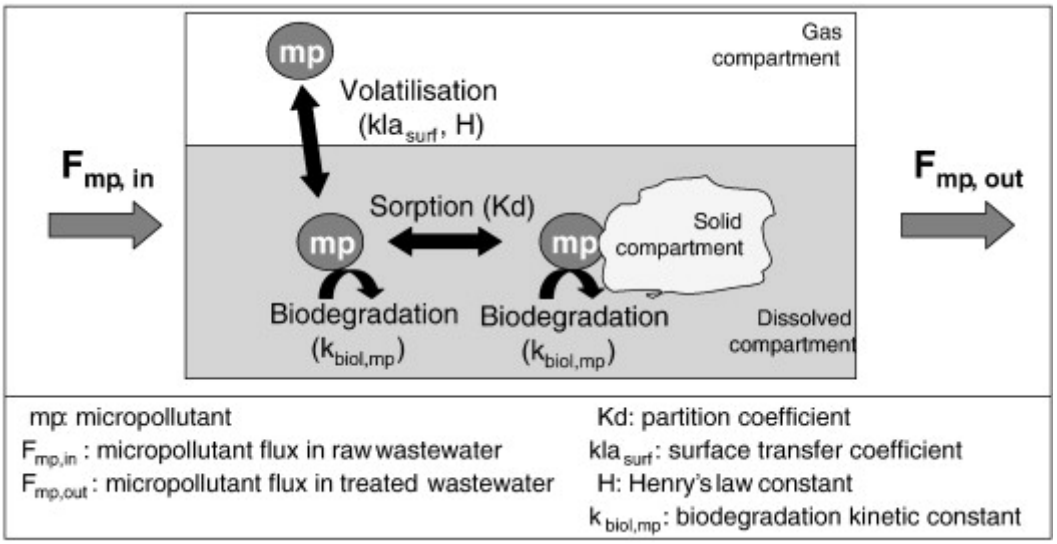

Figure 2.4 Fate of micropollutant in biological treatment (Pomiès et al. (2013))

2.5.1 Biodegradation process

The kinetic model to represent characteristics of biodegradation is described by the variations of PPCPs concentration dissolved in liquid phase. Biodegradation constant can be often expressed by a pseudo first-order kinetic in which the rate of biodegradation is directly proportional to the dissolved substance concentration, as described in following equation (Schwarzenbach et al., 2003):

$$\frac{\mathrm{dC}}{\mathrm{d}t} = -k_1 \cdot \mathrm{C} \leftrightarrow \mathrm{C}_t = \mathrm{C}_0 \cdot e^{-k_1 \cdot t} \qquad \text{(Eq.2.2)}$$

Where, K_1 is the first order rate constant (h^{-1}); C_0 is initial concentration of PPCPs (ng/L); and C_t is concentration of PPCPs at time t (ng/L). Using this equation, half-lives (h) can be calculated as (ln 2)/(k_1). Only dissolved concentrations had been considered in most studies on biodegradation of PPCPs (Joss et al., 2006; Wick et al., 2009; Plosz et al.,

2010).

On the other hand, Schönerklee et al. (2009) indicated modelling on biodegradation in pilot MBR process, assumed that biodegradation in the dissolved phase was achieved concurrently with the adsorbed phase. Urase et al. (2005) also suggested two-phase model, for which biodegradation was considered by adsorbed fraction using the transfer of the compounds between liquid phase and solid phase to elucidate the contribution of adsorption and that of degradation. Few biodegradation models have also been proposed to take into account the influence of substrate, for which biodegradation was considered as the growing process with microbial growth and utilization of substrate, which can be described by Monod-type kinetics, modelled with following equation (Pomiès et al., 2013):

$$\left(\frac{dC}{dt}\right) = \frac{1}{Y_p} \times \mu_{max,\,p} \left(\frac{S_O(t)}{K_{O,p} + S_O(t)}\right) \times \left(\frac{S_p(t)}{K_p + S_p(t)}\right) \times X_{MLSS} \quad \text{(Eq.2.3)}$$

Where,

Y_p: Coversion yield
$\mu_{max,p}$: Maximum growth rate (T^{-1})
S_O: Oxygen concentration ($M\ L^{-3}$)
$K_{o,p}$: Oxygen half saturation coefficient ($M\ L^{-3}$)
K_p: PPCPs half saturation coefficient ($M\ L^{-3}$)
X_{MLSS}: MLSS concentration ($M\ L^{-3}$)

In this case, however, because various parameters like specific growth rate, half saturation concentration and consideration of decay rate in addition to concentration of PPCPs are required, it has not been studied adequately and thus, further efforts are needed to achieve better knowledge on suitable biodegradation models for dealing with target compounds.

2.5.2 Transformation of parent compounds

There are circumstances where the effluent concentrations of some PPCPs such as diclofenac, carbamazepine and erythromycin were higher than their influent concentrations. This is because that the presence of some substances such as human

metabolites and transformation products in the influent, which can be transformed back to parent compounds during biological treatment (Göbel et al., 2007; Kasprzyk-Hordern et al., 2009; Luo et al., 2014). Also, some of these metabolites or by-products are biologically active and may even be more toxic than their parent compounds. Plosz et al. (2010) demonstrated the impacts of competitive inhibition and compound formation from several possible parent substances, for which antibiotics like sulfamethoxazole, ciprofloxacin and tetracycline were excreted as the parent compound, in conjugated form, or as oxidation or hydrolysis products. The similar behavior in another review have been reported that increased concentration of carbamazepine in effluent was contributed due to the conversion of carbamazepine glucuronides and other conjugated metabolites to the parent compound by enzymatic processes taking place in the treatment plant (Vieno et al., 2007). Botta et al. (2009) also indicated that glyphosate, which is used extensively as a non-selective herbicide, is biodegraded in aminomethylphosphonic acid (AMPA) which was suspected to be more toxic.

As mentioned above, in WWTPs, transformation of these parent compounds and other conjugated metabolites may have negative impacts on either discharge performance of effluent as well as the effect of biomass performance which is significantly associated with biodegradation, leading to have difficulty for creating models to predict fate of PPCPs

2.5.3 Cometabolism

In conventional biological process, microorganisms use organic matters as primary substrates for their cell growth and induce enzymes for their assimilation, which are known as metabolism (Tran et al., 2013). However, PPCPs are not a source of carbon or energy to maintain biomass growth because these micropollutants are commonly detected in waters at trace concentrations, ranging from a few ng/L to several µg/L, and thus a co-substrate like readily biodegradable organic matters or ammonium and another utilizable compound are necessarily required to serve as growth substrate and induce the corresponding enzymes for the biodegradation. This phenomenon is regarded as cometabolism. In other words, cometabolism is defined as the simultaneous degradation of two compounds, in which the degradation of the second compound (the secondary substrate) depends on the presence of the first compound (the primary substrate). The simultaneous degradation of the co-substrate and the PPCPs is linked to the capacity of the enzymes to degrade many substances (Dalton et al., 1982).

Table 2.3 Literature reviews of previous studies for cometabolic degradation

Categories	Compounds	Experimental conditions	Inhibition of activity	References
X-ray contrast	Iopromide	NAS[a]	ATU	Batt et al. (2006)
Antibiotics	Trimethoprim	NAS	ATU	Batt et al. (2006)
	Triclosan	NAS	ATU	Roh et al. (2009)
		(*N*. europaea[b])	H_2SO_4	
		Aerobic sludge	-	Kim et al. (2011)
Beta-blockers	Atenolol Metoprolol Sotalol	SBR[c]	ATU	Sathyamoorthy et al. (2013).
NSAIDs	Ibuprofen	NAS	ATU	Roh et al. (2009).
		(*N*. europaea)	H_2SO_4	
Estrogens	E1 E2 E3 EE2	NAS (*N*. europaea)	ATU	Shi et al. (2004)
EDCs	BPA	SBR	ATU	Kim et al. (2007)
		NAS	ATU	Roh et al. (2009)
		(*N*. europaea)	H_2SO_4	

[a] Nitrifying activated sludge, [b] *Nitrosomonas europaea*, and [c] Sequencing batch reactor.

E1:Estrone, E2: 17β-estradiol, E3: Estriol, and EE2: 17α-ethynylestradiol, and BPA: Bisphenol A .

For example, ammonia oxidizing bacteria (AOB) is known to catalyze the oxidation of a large variety of organic pollutants via AMO which is non-specific enzymes. As can be shown in Table 2.3, some reviews suggested that cometabolic biodegradation linked to AOB growth could significantly impact on the removal of selected beta blockers (Sathyamoorthy et al., 2013). Also, Khunjar et al. (2011) demonstrated effect of autotrophic and heterotrophic bacteria during biotransformation, for which different kinetics in accordance with each compound were found. Particularly, unlike autotrophic bacteria, heterotrophic bacteria can involve in both cometabolism and metabolism depending on the concentration of PPCP which are existed in the environment and their toxicity to the bacteria (Tran et al., 2013). Therefore, further study on the relative role of both autotrophic and heterotrophic bacteria should be investigated to understand

adjustable conditions in which target compounds are greatly biodegraded, which may prove useful insights into the cometabolic activities in terms of model development using biodegradation.

2.6 Summary

In this chapter, we summarized the reviews to compare and better understand overview of the completed studies on removal of PPCPs in WWTPs, the removal characteristics in MBR Process, the influence of coagulation on MBR process, and even modelling. The findings were as follow:

1) Even though there are several studies on removal of PPCPs in different WWTPs, very little information on removal characteristics of PPCPs in MBR process is still available.

2) Also, in MBR process, not only the removal mechanisms, including such as biodegradation and adsorption, but also evaluations on applicability of coagulation for effective removal of PPCPs are not sufficiently studied.

3) Recently, predictive models for removal of PPCs have been developed, but there is presently no consensus between them because they have been applied by various concepts. Therefore, it should be proposed to take in to account more suitable models in MBR process.

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Chapter Ⅲ

Comparison on Fate and Removal Characteristics of PPCPs between MBR and Various Biological Treatment Processes

3.1 Introduction

The world is facing a severe water shortage due to population growth, rapid urbanization, climate change and rising farming, particularly not only in water scarce regions but also in developed countries. In order to address these problems, the reuse of wastewater is absolutely necessary, which can lead to maintain sustainable water environment.

However, one of the key issues in wastewater reclamation is the emerging problem of micropollutants such as PPCPs and EDCs. Recently, more PPCPs are being released into wastewater via wash-off, urine, and feces, as parent compounds, conjugates or metabolites due to the increased consumption of PPCPs (Langford et al., 2009). This has triggered concern because in the environment, certain PPCPs are persistent and bioaccumulative, potentially producing human health and ecological impacts (Brausch et al., 2012). The occurrence of PPCPs in the aquatic environment is significant concern to public health and the environment because of the potential adverse impact on living organisms caused by these compounds, which can include a range of oestrogenic, mutagenic, endocrine disrupting and genotoxic effects (Stasinakis et al., 2010; Zhao et al., 2010; Gago-Ferrero et al., 2011). Adverse effects from the presence of PPCPs in the aquatic environment have been reported for bacterial, invertebrate, aquatic vertebrates, and algal populations in the receiving waters of wastewater treatment systems, which include WWTPs and on-site wastewater treatment systems (Du et al., 2014; Brodin et

al., 2013; Fatta-Kassinos et al., 2011).

Moreover, existing WWTPs which are mainly operated by CAS processes cannot completely eliminate these compounds, but in MBR process, removal performance of PPCPs as well as organic matters and nutrients is efficiently achieved and therefore, they have become an alternative to CAS processes for wastewater treatment. Compared with CAS process, one of the advantages of MBR is to act as a barrier for PPCPs and prevent the discharge of potentially detrimental compounds into the water environment. Many studies have focused on occurrence and removal of PPCPs all over the world, but there is little information of PPCPs fate and comparative evaluation for efficient treatment processes. Therefore, it needs to investigate their behaviors and concentrations to grasp how their removal is influenced by MBR process, with various treatment processes in different WWTPs.

In Chapter III, MBR process and various treatment technologies at different WWTPs were investigated to compare occurrence, fate and removal performance of PPCPs. Also, comparative study on removal characteristics between studied WWTPs and lab-scale MBR process was evaluated using mass balance of PPCPs removal, thereby elucidating the contribution of removal mechanisms. This study may be critical to decide appropriate processes for minimizing risk from emissions of PPCPs into the water environment.

3.2 Materials and methods

3.2.1 Chemicals and standards

Based on the consumption and usage of PPCPs total 57 compounds were selected as the target compounds in this study (non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, antibiotics, antibacterials and etc.). Specific categories and classes of selected compounds are shown in Table 3.1. Also, the concentrations of stock solutions of the PPCPs ranging from about 100 to 1,000 mg/L had an isotopic purity greater than 98%. They were prepared with methanol because of their low solubility in water and stored at -30°C in the dark.

Table 3.1 Target compounds in this study

Categories	Classes	Compounds	
NSAIDs		Antipyrine	Ketoprofen
(Non-steroidal anti-inflammatory drugs)		Diclofenac	Mefenamic_acid
		Fenoprofen	Naproxen
		Indometacin	
Analgesics		Acetaminophen	Isopropylantipyrine
		Ethenzamide	
Antibiotics	Macrolide	Azithromycin	Roxithromycin
		Clarithromycin	Tylosin
	Tetracyclines	Chlortetracycline	Tetracycline
		Oxytetracycline	
	Pleuromutilin	Tiamulin	
	Chloramphenicol	Thiamphenicol	
	Lincosamide	Lincomycin	Trimethoprim
Antipruritic		Crotamiton	
Decongestant		Clenbuterol	
Antibacterials	Sulfonamide	Sulfadimethoxine	Sulfamonomethoxine
		Sulfadimidine	Sulfapyridine
		Sulfamerazine	Sulfathiazole
		Sulfamethoxazole	
	Fluoroquinolone	Ciprofloxacin	Levofloxacin
		Enrofloxacin	Norfloxacin
Antiarrhythmic Agents	Beta blocker	Atenolol	Propranolol
		Metoprolol	
		Disopyramide	Diltiazem
Anticonvulsants		Carbamazepine	Primidone
BLLAs		Bezafibrate	Clofibric_acid
(Blood lipid lowering agents)			
Stimulant		Caffeine	
Diuretic		Furosemide	
Antifungals		Griseofulvin	Triclosan
		Triclocarban	
β2-receptor		Salbutamol	
Atypical antipsychotic		Sulpiride	
Insect repellent		DEET[#1]	
Veterinary medicine		Tylosin	Ifenprodil
Others		2QCA[#2]	Pirenzepine
		Cyclophosphamide	Theophylline
		Dipyridamole	

DEET[#1]: N,N-Diethyl-meta-toluamide and 2QCA[#2]: 2_quinoxalinecarboxylicacid

3.2.2 Analytical methods

Liquid samples were filtrated through the glass fiber filter (Whatman GF/B, 1 μm). EDTA-2Na of 1 g/L and a mixture of surrogate standard were added after filtration. The extraction process was performed using solid phase extraction (SPE) with Oasis HLB (Waters, 200mg, 6cc), in which the cartridges were conditioned by releasing methanol and distilled water. After completing concentration by cartridges, they were eluted with methanol and dried by nitrogen draft system.

Since solid samples consisted of various structures and chemical properties they were pretreated simultaneously to extract individual PPCPs adsorbed to sludge at three pH levels (pH 2, 7 and 11) and mixed in methanol in a 9:1 (v/v) ratio. Ultrasonication (As one, ASU-20D) and centrifuge (Kubota, Centrifuge 4000) were repetitively used to collect supernatant of solid samples. And then, it was evaporated to dry and redissolved in 1 mL of mixture of formic acid and methanol. The 1 mL final extract was used for LC-MS/MS (UPLC (AQUITY, Waters), MS/MS (Quattro micro API, Waters)). The method using the recovery correction which was calculated from the difference between two aliquots from one sample with and without addition of target PPCPs mixture, and the internal standard method by appropriate surrogate standards were used for the quantification for the samples, respectively (Kim et al., 2012; Narumiya et al., 2013).

In addition to analysis of PPCPs, water quality of WWTPs such as biochemical oxygen demand (BOD_5), chemical oxygen demand (COD_{cr}), total suspended solids (TSS), total nitrogen (TN) and total phosphorus (TP) was analyzed according to the standard methods (APHA, 2005). Operating parameters such as dissolved oxygen (DO), pH, temperature and oxidation-reduction potential (ORP) were measured by portable sensor (Horiba, D-50 and 55).

3.2.3 Specification of WWTPs and sampling points

Sampling events were conducted at four WWTPs which are located in close to the Seoul city, Korea from June, 2014 to May, 2015. The process diagrams and the various sampling points of WWTPs are shown in Figure 3.1, and the details about main processes, influent sources, population served and inflow rate are summarized in Table 3.2.

WWTP-A consisted of two main streams such as domestic treatment (Figure 3.1 (a), henceforth WWTP-A (D)) and industrial treatment (Figure 3.1 (b), henceforth WWTP-A (I)), in which two processes are almost similar except for disinfection system. The Main

process of WWTP-A is Symbio technology that allows nitrification and denitrification to occur simultaneously in the same reactor. It uses measurement of the intracellular pool of reduced nicotinamide adenine dinucleotide (NADH) for assessing the real-time biological activity in activated sludge systems. This information is used to control the air supply in the aeration tank to maintain DO at the desired low level, which ensures that both anoxic and aerobic zones are developed in sludge flocs (Trivedi, 2009).

WWTP-B uses 5-stage biological nutrient removal (BNR) process that is an expansion of the classic four stage approach, with the pre-anoxic tank to efficiently achieve denitrification and phosphorous removal without supplying additional carbon source. Liquid and solid samples in each reactor and effluent after ultraviolet (UV) disinfection were collected.

WWTP-C is operated by A2O process that includes anaerobic, anoxic and aerobic tanks. Samples were collected not only in reactors, primary and excess sludge, but also effluent after ozonation to evaluate untreated PPCPs in biosolids and post treatment after biological treatment process. Specifically, land application of reclaimed water and biosolids might lead to contamination of soil and groundwater; recently, PPCPs were found in recycled organic manure produced from sewage sludge (Motoyama et al., 2011).

WWTP-D includes MBR Process and coagulation for phosphorus removal where membrane is fully immerged in aerobic tank with internal recycle is operated by 3Q to remove nitrogen and buffer high MLSS concentration for stabilization of biomass.

Table 3.2 Characteristics of WWTPs

Characteristics	WWTPs				
	WWTP-A (D) (n=4)	WWTP-A (I) (n=4)	WWTP-B (n=3)	WWTP-C (n=7)	WWTP-D (n=4)
Influent source	Domestic	Industrial	Domestic	Domestic	Domestic
Main process	Symbio	Symbio	5-stage BNR	A2O	MBR
Inflow rate (m^3/d)	409,500	409,500	36,800	384,000	3,200
Inhabitants	762,915	762,915	114,993	1,033,305	7,503

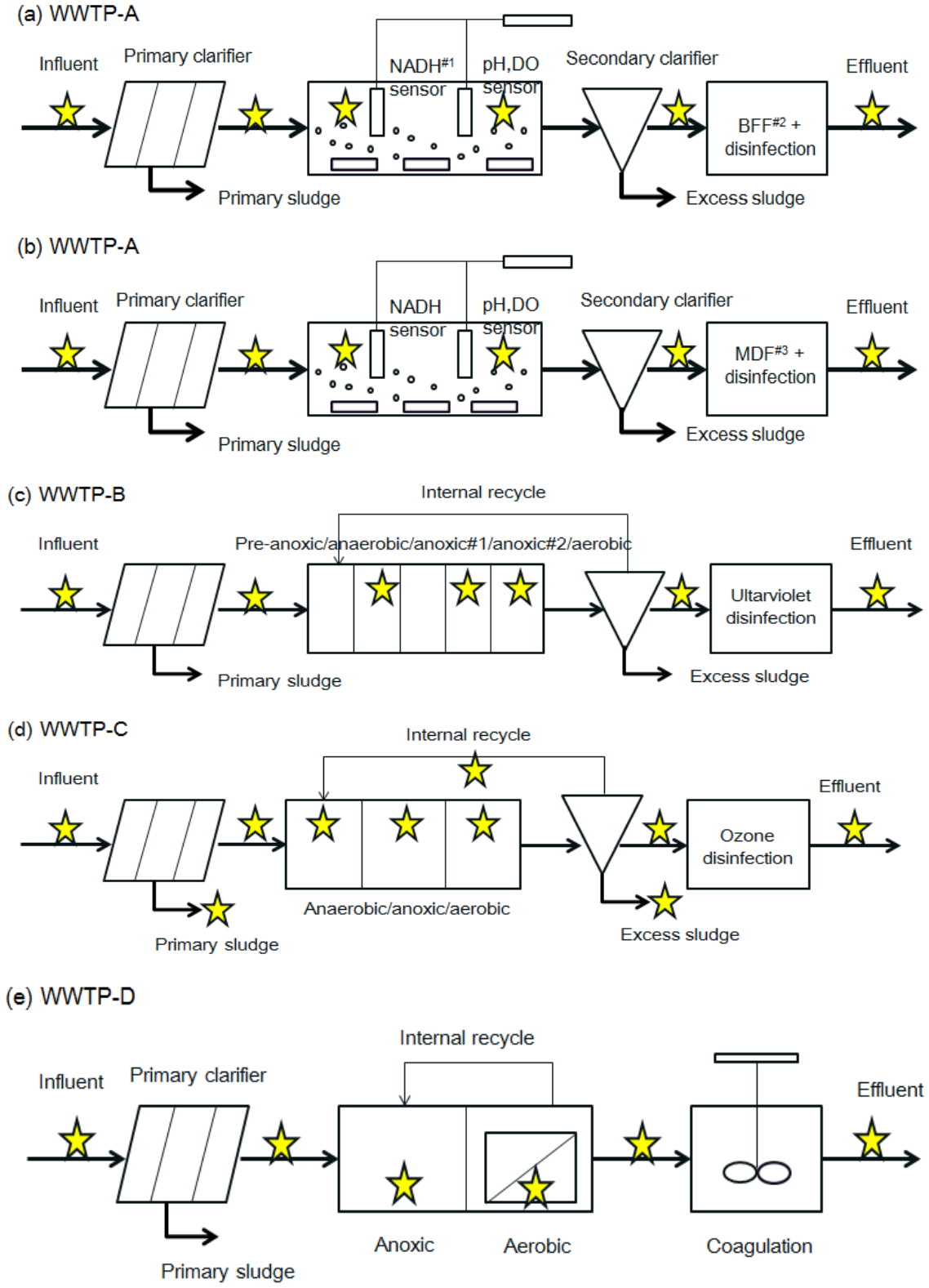


Figure 3.1 Process diagram and sampling points of WWTPs

(a) Domestic wastewater and (b) industrial wastewater

[#1] NADH: Nicotinamide adenine dinucleotide, [#2] BFF: Biological fixed film and [#3] MDF: Micro disc filter

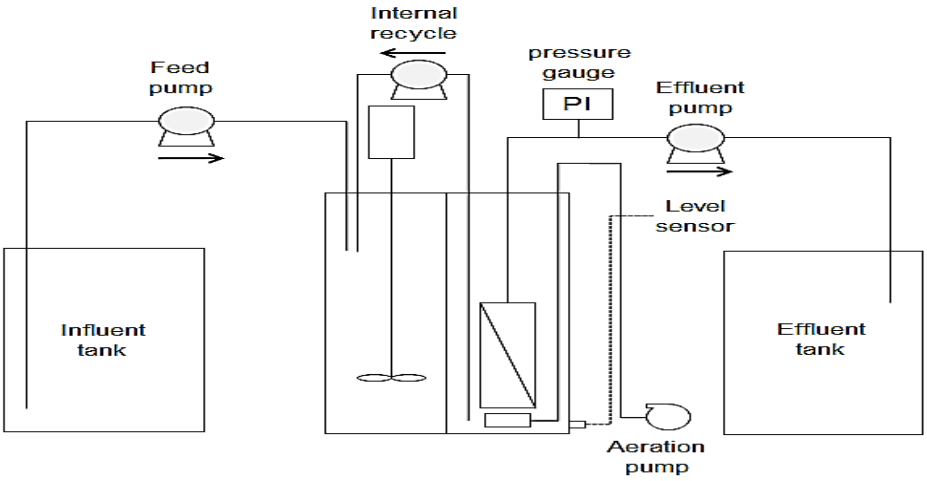


Figure 3.2 Schematic diagram of lab-scale MBR

3.2.4 Lab-scale MBR

Lab-scale study was performed to evaluate removal mechanisms on removal of PPCPs and to compare mass balance between lab-scale MBR and other WWTPs. Specification on membrane and operating conditions of lab-scale MBR are represented in Table 3.3 and schematic diagram of process is shown in Figure 3.2. Lab-scale MBR with a reactor volume of 5 L was operated for 1 year and consisted of two main reactors (anoxic and aerobic tank in which membrane module was submerged). Activated sludge from aerobic tank of WWTP-C was used to inoculate the reactor until a target MLSS concentration is reached. The influent of WWTP-C (after coarse screen) was provided continuously by a peristaltic pump. Also, mixing by vertical stirrer in anoxic tank and air supply to maintain aerobic condition in aerobic tank was employed, respectively. In aerobic tank, internal recycle (3Q) from aerobic to anoxic tank was applied to efficiently remove nitrogen and level sensor was used to control level of reactor volume. To prevent membrane surface from accumulating particles and foulants, effluent pump was operated by 7 min of operation and 1 min of relaxation, in which pressure sensor was set for TMP monitoring.

The target range of the MLSS concentration was 7,000-11,000 mg/L and if necessary, the excess sludge was extracted for analysis of water quality or PPCPs. Lab-scale MBR was operated with average temperature 25 ℃ (±5 ℃) and average pH 6.8 (±0.4). Even though operating conditions like HRT and F/M ratio were flexibly adjusted by experimental design and seasonal effect, their initial values were set as 11 hour and 0.1g BOD/g MLVSS/d, respectively.

Table 3.3 Specification of lab-scale MBR

Parameters	Specification
Membrane type	Microfiltration (MF)
Module type	Hollow fiber
Membrane material	Polyvinylidene fluoride (PVDF)
Pore size	0.4 μm
Surface area	0.02 m^2 x 2
Effluent cycle	Operation - 7 min, stop - 1min
Aeration rate	4 L/min
Internal recycle	3Q

3.2.5 Calculations of mass balance

The elimination of PPCPs during wastewater treatment processes can occur via biodegradation, adsorption onto sludge, photodegradation and volatilization. As mentioned in chapter 2.2, however, latter two pathways are not considered significantly in WWTPs. Therefore, biodegradation and adsorption are assumed to be the primary removal mechanisms for the removal of target compounds. The calculation of mass balance was based on the following equations (Guerra et al., 2014):

$$M_{inf} = M_{eff} + M_{bio} + M_{adsorp} \quad \text{(Eq.3.1)}$$

where,

M_{inf} (g/d) = Flow rate (m^3/d) x Influent PPCPs concentration (ng/L) x 10^{-6}
M_{eff} (g/d) = Flow rate (m^3/d) x Effluent PPCPs concentration (ng/L) x 10^{-6}
M_{adsorp} (g/d) = Sludge production rate (m^3/d) x Sludge PPCPs concentration (ng/L) x 10^{-6}
M_{bio} (g/d) was calculated by Eq.3.1 using mass loading in influent, effluent and adsorption i.e. $M_{bio} = M_{nf} – (M_{eff} – M_{adsorp})$

The degree of removal for biodegradation and adsorption were calculated using following equations:

$$\%R_{bio} = (M_{bio}/M_{inf}) \times 100 \quad \text{(Eq.3.2)}$$

$$\%R_{adsorp} = (M_{adsorp}/M_{inf}) \times 100 \quad \text{(Eq.3.3)}$$

3.3 Results and discussion

3.3.1 Results of water quality

As shown in Table 3.4 the water quality of each WWTP is summarized. For the removal of organic pollutants such as COD_{cr} and BOD_5, high removal performance was achieved in all WWTPs with above 92% in COD_{cr} or 97% in $BOD_{5.}$ For removal of nutrients like nitrogen and phosphorus, their removals over 83% in TN and 88% in TP were obtained, respectively. Even though relatively higher COD_{cr} and TN concentration was measured in influent source of WWTP-A (I) compared with other WWTPs, the removal efficiency was not reduced in COD_{cr} concentration. NH_3-N concentration of effluent was detected at somewhat high level. Typical MLSS concentration was measured in aerobic conditions of the surveyed WWTPs except for WWTP-D, in which high MLSS concentration was applied to maintain advantages of MBR process.

The results of water quality of various WWTPs showed that whole WWTP processes including physical and biological treatment were normally operated during sampling events and achieved stable removal performance. It can be supported by these data that our study on fate and removal of PPCPs in each WWTP was carried out at normal operating conditions.

3.3.2 Occurrence of PPCPs in WWTPs

3.3.2.1 Mass loading rate

Mass loading rate of PPCPs was calculated by detected concentration of individual compounds and inflow rate. PPCPs mass loading rate of influent for each target compound is represented in Figure 3.3 and Figure 3.4 shows the sum of each category. The fourth most concentrated compounds were acetaminophen, caffeine, naproxen and theophylline (e.g., the range of acetaminophen between 41% and 71%, caffeine between 11% and 28%, naproxen between 2% and 5% and theophylline between 2% and 22%). One possible reason for the high levels of these compounds may be their accessibility and extensive use by consumers (Jelic et al., 2011). Similar results on high levels of acetaminophen, naproxen and caffeine were reported in WWTPs of North American and Canada (Lishman et al., 2006; Conkle et al., 2008; Behera et al., 2011; Guerra et al., 2014). In addition to four compounds, antibacterials such as levofloxacin and ciprofloxacin, macrolide and tetracycline antibiotics were detected in each WWTP.

Table 3.4 Water quality of each WWTP

Parameters	WWTP-A (domestic)			WWTP-A (industrial)			WWTP-B			WWTP-C			WWTP-D		
	Inf. (mg/L)	Eff. (mg/L)	Rem. (%)	Inf. (mg/L)	Eff. (mg/L)	Rem. (%)	Inf. (mg/L)	Eff. (mg/L)	Rem. (%)	Inf. (mg/L)	Eff. (mg/L)	Rem. (%)	Inf. (mg/L)	Eff. (mg/L)	Rem. (%)
COD_{cr}	259.5 (±31.5)	20.7 (±4.5)	92.0 (±2.5)	741.2 (±87.6)	21.2 (±2.8)	97.1 (±1.5)	301.2 (±41.3)	16.1 (±10.8)	94.6 (±4.1)	275.5 (±96.3)	10.3 (±8.1)	96.3 (±2.1)	307.2 (±20.2)	23.0 (±5.1)	92.5 (±3.8)
BOD_5	108.7 (±16.2)	1.1 (±0.4)	98.9 (±0.4)	285.0 (±61.5)	1.8 (±0.5)	99.3 (±0.2)	220.1 (±50.0)	4.2 (±78.3)	98.1 (±1.2)	133.2 (±43.3)	1.5 (±1.3)	98.8 (±1.0)	101.3 (±28.1)	2.2 (±1.2)	97.8 (±1.5)
TSS	130.9 (±22.4)	2.6 (±4.5)	98.0 (±1.1)	520.0 (±78.3)	4.8 (±2.7)	99.1 (±0.3)	162.0 (±150.5)	4.0 (±2.5)	97.5 (±2.0)	159.0 (±105.5)	4.5 (±1.5)	97.2 (±1.8)	118.0 (±32.1)	6.1 (±2.5)	94.8 (±2.0)
MLSS	3070 (±214)		-	4860 (±274)		-	2790 (±612)		-	3500 (±415)		-	13510 (±1560)		-
MLVSS	2450 (±101)			3820 (±91)			2210 (±205)			2825 (±150)			10550 (±1100)		
NH_3-N	23.8 (±5.5)	1.5 (±0.8)	93.7 (±2.1)	22.3 (±6.1)	4.8 (±2.0)	78.5 (±4.2)	24.6 (±7.0)	0.8 (±0.4)	96.7 (±1.9)	18.0 (±8.1)	0.2 (±0)	98.9 (±0.4)	18.6 (±5.5)	0.9 (±0.3)	95.1 (±2.4)
TN	35.9 (±7.2)	5.2 (±3.1)	85.5 (±10.1)	59.9 (±8.8)	8.6 (±2.7)	85.6 (±3.3)	49.5 (±6.9)	6.8 (±4.2)	86.2 (±5.1)	41.2 (±6.3)	3.9 (±4.4)	90.5 (±5.2)	31.7 (±4.8)	3.9 (±2.7)	87.7 (±4.0)
TP	3.8 (±2.1)	0.3 (±0.2)	92.1 (±4.3)	10.3 (±3.9)	0.5 (±0.2)	95.1 (±2.8)	5.1 (±2.1)	0.3 (±0.1)	94.1 (±2.3)	3.5 (±2.4)	0.4 (±0.3)	88.5 (±5.1)	2.9 (±1.8)	0.2 (±0.1)	93.1 (±1.2)

Inf.: Influent, Eff.: Effluent and Rem.: Removal efficiency. Data of MLSS and MLVSS shows concentration in aerobic condition.

Also, standard deviation of concentration and percentage are given in brackets.

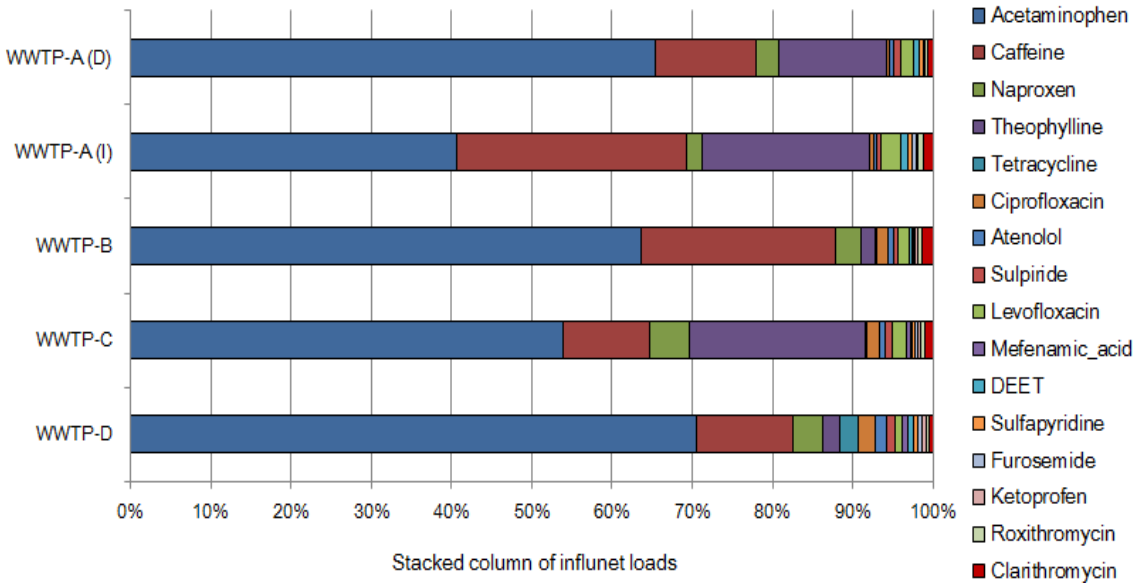


Figure 3.3 PPCPs mass loading rate in influent for each compound

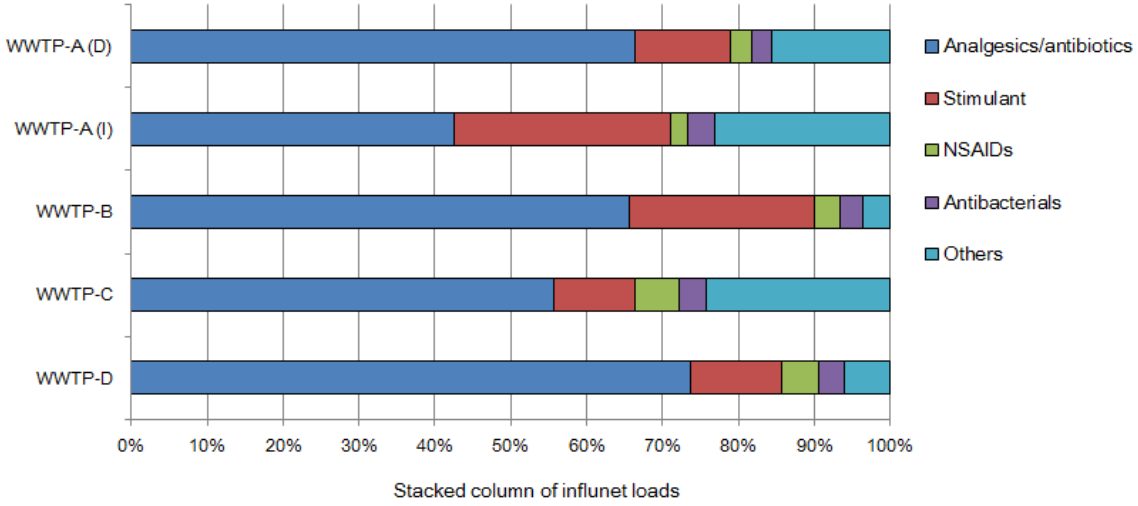


Figure 3.4 PPCPs mass loading rate in influent for each category

In aspect of each group, analgesics and antibiotics were observed at the highest level, and their mass loading rate including stimulant, NSAIDs, and antibacterials accounted for median 85% of all WWTPs (e.g., 84% in WWTP-A (D), 77% in WWTP-A (I), 96% in WWTP-B, 76% in WWTP-C and 94% in WWTP-D). Our study from some WWTPs was consistent with previous report. Kim et al. (2014) suggested the combined concentrations of target compounds, which belong to analgesic/anti-inflammatories, psychomotor stimulants, and antidiabetic categories, accounted for 96%. Although the high mass loading rate of compounds including these categories were detected,

WWTP-A (I) showed a relatively low loading rate due to ratio decrease of frequently detected compounds in influent by industrial or livestock sources. Various PPCPs were found in WWTP-C which is designed to deal with the metropolitan area of Seoul, South Korea. Among several compounds detected at high level, loading rate of theophylline, which is used together with other medicines to treat the symptoms of asthma, was much higher in WWTP-C. Previously, Kim et al. (2013) reported that among the target PPCPs, acetaminophen with 74.5 μg/L, caffeine with 25.1 μg/L, ibuprofen with 9.5 μg/L, naproxen with 5.9 μg/L and theophylline 4.1 μg/L were detected in the highest levels in the WWTP influent of Korea.

3.3.2.2 Per capita loads

Total per capita loads were investigated to assess the fate of PPCPs during wastewater treatment process and removal tendency of each WWTP and other countries. Loads of PPCPs and total per capita loads are shown in Figure 3.5 and 3.6, respectively. While the total amount of PPCPs in influent of WWTP-A (D) and WWTP-C that served a large population was higher than that in other WWTPs that served a small population, total per capita loads of influent in individual WWTPs were similar except for the WWTP-A (I). The total per capita loads in influent ranged from 9.7 g d^{-1} 1000 $inhabitants^{-1}$ to 28.5 g d^{-1} 1000 $inhabitants^{-1}$ and the highest loads were found in WWTP-A (D). Also, their removals showed 95% in WWTP-A (D), 92% in WWTP-A (I), 93% in WWTP-B, 96% in WWTP-C and 95% in WWTP-D. These results indicated the higher removal efficiency compared with another study. For example, Qi et al. (2015) reported that the total loads of 27 pharmaceuticals and household chemicals ranged from 7.8-12.0 g d^{-1} 1000 $inhabitants^{-1}$ in the WWTP influents and were eliminated by 70-80% during the treatment processes. However, there was no significant difference between our study and those reported by Italy and Switzerland for the case of bezafibrate, carbamazepine, mefenamic acid and diclofenac (Castiglioni et al., 2006; Hollender et al., 2009).

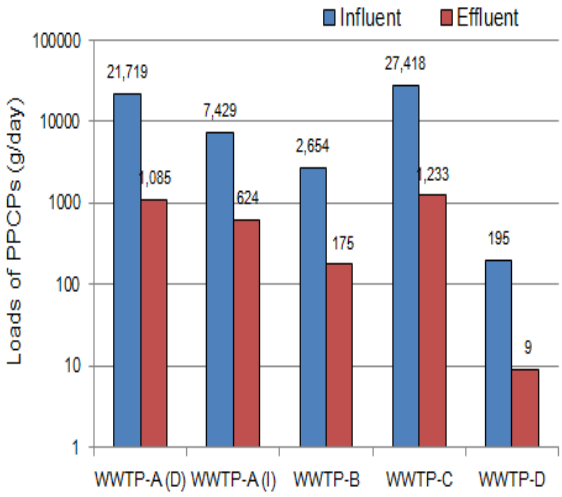


Figure 3.5 Loads of PPCPs

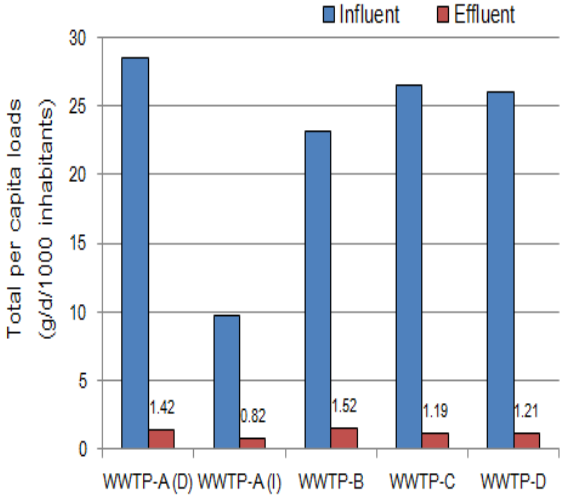


Figure 3.6 Total per capita loads

3.3.3 Removal of PPCPs in WWTPs

3.3.3.1 Removal by biological treatment

Overall removal efficiencies of target compounds in each WWTP were calculated using concentrations of influent and effluent from individual biological treatment processes. To understand the fate and removal characteristics of PPCPs in various biological treatments, not only concentration of influent and effluent, but also removal efficiency of the compounds were investigated (Table 3.5). For the compounds that were frequently detected in all WWTPs such as acetaminophen, caffeine, naproxen, and theophylline, over 90% of these compounds were highly eliminated by biological treatment processes (except for 84% of naproxen removal in WWTP-A (I)). The removal efficiencies of acetaminophen and caffeine were quite similar to the other studies, but the removal of naproxen was higher in this study (Yu et al., 2006; Radjenovic et al., 2007; Radjenovic et al., 2009). The second highest group of PPCPs in influent was fluoroquinolone antibacterials, with ranging from 100 to 1,500 ng/L. These PPCPs, ranked from the highest to the lowest, include ciprofloxacin and levofloxacin. According to a recent review by Guerra et al. (2014), levels of antibiotics ranged between 1.1 and 3,100 ng/L, in which the highest levels were observed for ciprofloxacin (17-2,500 ng/L). In our study, for removal of these compounds, a relatively higher removal performance was achieved in WWTP-C and WWTP-D, for which 86% or 82% in the removals of levofloxacin and 92% or 94% in the removals of ciprofloxacin were shown, while their

removals were the lowest in WWTP-B.

Table 3.5 Fate and removal of PPCPs by biological treatment

Compounds	WWTP-A (D)					WWTP-A (I)					WWTP-B				
	Inf. (ng/L)	± SD	Eff. (ng/L)	± SD	Removal (%)	Inf. (ng/L)	± SD	Eff. (ng/L)	± SD	Removal (%)	Inf. (ng/L)	± SD	Eff. (ng/L)	± SD	Removal (%)
Acetaminophen	33712	3604	35	27	99.9	7120	6271	58	88	99.2	44480	6313	15	21	100.0
Caffeine	6485	151	170	199	97.4	4998	2937	249	156	95.0	16961	2489	114	66	99.3
Naproxen	1438	619	59	21	95.9	355	224	57	64	84.0	2218	812	74	52	96.7
Theophylline	6952	7984	167	351	97.6	3658	4878	133	101	96.4	1224	145	32	23	97.4
Levofloxacin	827	124	260	30	68.6	446	155	136	201	69.5	914	296	531	279	41.9
Ciprofloxacin	210	120	26	44	87.5	97		<LOQ			1061	189	406	193	61.8
Sulpiride	479	82	318	210	33.6	100	50	33	20	67.6	422	202	335	420	20.6
Clarithromycin	360	337	166	51	53.7	219	172	50	47	77.3	1001	4	367	192	63.3
Triclocarban	NA		NA			NA		<LOQ			801	120	200	101	75.0
Atenolol	231	327	166	200	28.1	41	58	<LOQ			439	75	379	266	13.7
Mefenamic_acid	NA		<LOQ			NA		<LOQ			481	221	251	55	47.8
Bezafibrate	266	154	42	77	84.4	52	37	7	5	85.9	290	81	55	37	81.0
Roxithromycin	114	87	101	3	11.0	99	52	24	16	76.1	348	135	217	122	37.6
Azithromycin	56	5	52	6	6.6	18	4	14	7	23.5	85		56	40	33.5
Furosemide	68	96	52	35	23.7	99		<LOQ			117	27	87	118	25.5
Ketoprofen	40	27	14		65.1	45	9	18		59.9	216	27	160	111	25.9
Sulfapyridine	263	69	140	70	46.6	77	18	8		90.0	153	39	<LOQ		
Lincomycin	46		19		59.2	13		9		29.5	122		NA		
Sulfamethoxazole	193	269	149	58	22.7	75	12	14		81.8	240	23	196	207	18.4
Diclofenac	54	77	<LOQ			<LOQ		<LOQ			78	7	123	83	-58.6
DEET	376	389	273	34	27.4	153	134	90	19	41.2	271	189	234	284	13.7
Carbamazepine	160	150	121	19	24.2	101	22	30	14	70.0	102	19	136	96	-33.6
Tetracycline	24		NA			NA		NA			81	30	30	18	62.8
Crotamiton	178	132	133	100	25.2	98	36	47	32	51.9	152	15	130	129	14.6
Trimethoprim	109	7	84	43	23.0	33	14	14		57.1	230	11	158	111	31.4
Triclosan	NA		<LOQ			NA		<LOQ			299	105	144	34	51.9
Diltiazem	20	29	24	6	-15.8	7	3	3	2	53.4	56	13	50	33	11.7
Propranolol	19	13	30	3	-58.0	8		5	2	38.6	17	1	NA		
Norfloxacin	34		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Indometacin	7	10	<LOQ			<LOQ		<LOQ			8		6	1	29.2
Primidone	12	2	<LOQ			<LOQ		315			<LOQ		22		
Oxytetracycline	60		<LOQ			NA		<LOQ			<LOQ		<LOQ		
Sulfamerazine	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Antipyrine	<LOQ		13			<LOQ		<LOQ			<LOQ		<LOQ		
2QCA	<LOQ		23	3		<LOQ		13			<LOQ		<LOQ		
Isopropylantipyrine	46	37	21	10	54.3	61	23	24		60.3	6	6	5	3	15.9
Metoprolol	0		4			<LOQ		7			10	11	8	6	14.9
Salbutamol	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Sulfathiazole	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Clofibric_acid	8	11	4		46.0	NA		<LOQ			0		<LOQ		
Chlortetracycline	NA		NA			NA		<LOQ			<LOQ		<LOQ		
Thiamphenicol	184	158	41	60	77.9	26		<LOQ			<LOQ		<LOQ		
Sulfadimidine	9	0	6		41.2	<LOQ		<LOQ			<LOQ		<LOQ		
Pirenzepine	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Sulfamonomethoxine	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Enrofloxacin	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Clenbuterol	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Disopyramide	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Ethenzamide	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		NA		
Sulfadimethoxine	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Cyclophosphamide	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		3	2	
Ifenprodil	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Tiamulin	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Dipyridamole	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		NA		
Tylosin	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Griseofulvin	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Fenoprofen	<LOQ		<LOQ			6		<LOQ			<LOQ		<LOQ		

Inf.: Influent concentration, Eff.: Effluent concentration, SD: Standard deviation and Removal: Removal efficiency. Also, <LOQ and NA indicate limit of quantification and not available by low recovery rate, respectively.

(Continued)

Compounds	WWTP-C					WWTP-D					Lab-scale				
	Inf. (ng/L)	± SD	Eff. (ng/L)	± SD	Removal (%)	Inf. (ng/L)	± SD	Eff. (ng/L)	± SD	Removal (%)	Inf. (ng/L)	± SD	Eff. (ng/L)	± SD	Removal (%)
Acetaminophen	37172	21263	14	5	100.0	42337	14933	63	68	99.9	10471	11501	21	24	99.8
Caffeine	7355	885	16	5	99.8	7237	3692	147	258	98.0	5075	3214	146	141	97.1
Naproxen	3390	1308	34	48	99.0	2195	1644	75	154	96.6	2696	1293	55	90	98.0
Theophylline	15219	6458	21	17	99.9	1349	382	111	72	91.8	1562	2214	60	42	96.1
Levofloxacin	1187	448	171	34	85.6	513	268	94	46	81.7	1430	452	236	75	83.5
Ciprofloxacin	1042	371	88	33	91.6	1257	1232	73	214	94.2	1363	574	155	47	88.7
Sulpiride	625	200	575	104	8.0	682	17	788	96	-15.5	794	230	744	130	6.3
Clarithromycin	720	336	327	128	54.6	265	27	180	118	32.0	719	293	384	210	46.6
Triclocarban	541	319	10	2	98.2	40		<LOQ			529	447	8	5	98.5
Atenolol	487	303	338	50	30.6	856	133	129	48	85.0	489	149	213	120	56.4
Mefenamic_acid	354	341	199	32	43.8	427	154	152	84	64.3	467	219	116	25	75.1
Bezafibrate	340	101	85	69	74.8	72	79	15	25	79.0	353	152	25	27	93.0
Roxithromycin	298	70	147	23	50.8	266	92	119	44	55.4	349	114	170	53	51.3
Azithromycin	319	524	45	27	85.9	NA		8	2		275	196	73	44	73.3
Furosemide	205	91	147	66	28.6	321	69	101	35	68.6	263	51	84	65	67.9
Ketoprofen	266	41	85	44	68.2	304	32	52	9	82.9	261	40	29	25	88.8
Sulfapyridine	238	136	225	49	5.8	328	34	147	56	55.3	186	84	135	45	27.2
Lincomycin	153	146	101	88	34.1	5	7	3	4	37.0	177	106	21	26	88.4
Sulfamethoxazole	225	42	94	23	58.2	19	5	18	8	6.9	174	76	60	17	65.7
Diclofenac	113	69	168	34	-48.9	190	70	224	104	-18.0	170	16	106	43	37.5
DEET	212	77	42	19	80.0	373	445	276	79	26.0	148	81	54	43	63.5
Carbamazepine	129	65	145	95	-12.7	234	38	174	56	25.5	140	37	154	33	-10.2
Tetracycline	112	79	17	11	84.8	1344	421	4	8	99.7	120	45	15	10	87.5
Crotamiton	112	105	106	75	5.4	165	128	79	30	52.3	91	30	71	30	22.4
Trimethoprim	78	41	49	32	37.4	9		8	2	8.5	87	31	66	37	24.3
Triclosan	243	212	52	15	78.6	NA		<LOQ			85	164	23	13	72.5
Diltiazem	85	27	43	7	49.3	122	10	21	25	82.7	78	23	36	20	54.7
Propranolol	34	18	28	12	15.6	16	2	<LOQ			48	25	28	16	41.6
Norfloxacin	43	35	6	1	86.8	<LOQ		3			26	39	8	4	70.2
Indometacin	17	22	6	3	61.5	5	26	<LOQ			24	21	6	4	75.2
Primidone	18	7	16	5	10.6	<LOQ		<LOQ			22	5	21	5	8.5
Oxytetracycline	21	18	3	2	83.4	NA		1			19	19	2	1	87.0
Sulfamerazine	<LOQ		<LOQ			<LOQ		<LOQ			13	9	1	1	93.3
Antipyrine	14	15	13	4	9.6	<LOQ		<LOQ			10	3	12	3	-13.9
2QCA	<LOQ		<LOQ			<LOQ		<LOQ			10	5	8	3	23.1
Isopropylantipyrine	8	5	<LOQ			<LOQ		<LOQ			10	3	8	2	15.9
Metoprolol	3	3	5	1	-64.4	<LOQ		<LOQ			6	4	4	1	38.0
Salbutamol	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Sulfathiazole	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Clofibric_acid	<LOQ		<LOQ			<LOQ		<LOQ			NA		<LOQ		
Chlortetracycline	<LOQ		<LOQ			NA		<LOQ			NA		<LOQ		
Thiamphenicol	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Sulfadimidine	<LOQ		<LOQ			9	6	5		48.5	<LOQ		<LOQ		
Pirenzepine	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Sulfamonomethoxine	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Enrofloxacin	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Clenbuterol	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Disopyramide	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Ethenzamide	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Sulfadimethoxine	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Cyclophosphamide	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Ifenprodil	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Tiamulin	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Dipyridamole	<LOQ		NA			<LOQ		<LOQ			<LOQ		<LOQ		
Tylosin	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Griseofulvin	<LOQ		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		
Fenoprofen	2		<LOQ			<LOQ		<LOQ			<LOQ		<LOQ		

Among the compounds having more than 100 ng/L concentrations, removal performance of bezafibrate and ketoprofen was higher than other PPCPs in all of the studied WWTPs. Average removal efficiencies of two compounds were 81% of bezafibrate and 60% of ketoprofen. Meanwhile, the effluent concentrations of

carbamazepine, diclofenac and diltiazem were much higher than influent concentrations. It has been reported that their concentrations were hardly eliminated during biological treatment processes and it could be explained by the presence of input conjugate compounds of carbamazepine that are being retransformed during treatment process into the original compounds. Also, diclofenac and clofibric acid, lipid regulator, were found to be slightly recalcitrant pharmaceutical residues in some studies (Petrovic et al., 2009). Kimura et al. (2005) demonstrated the persistence of diclofenac and clofibric acid in both systems like MBR and CAS because of the presence of chlorine in their structures, which makes them hardly degradable.

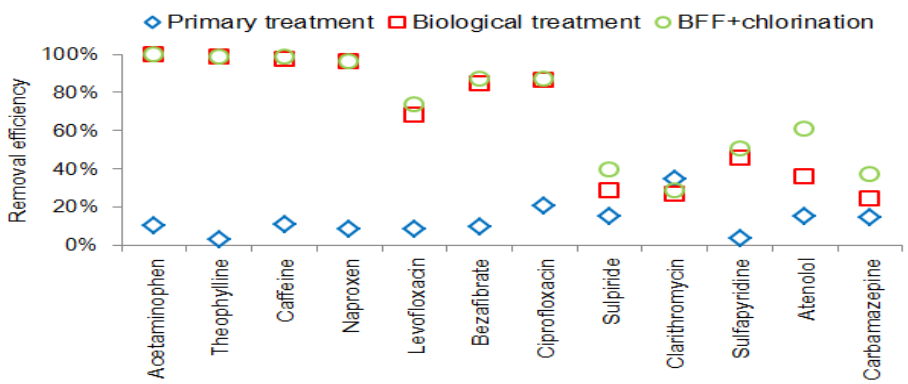
For all studied WWTPs, better removal were obtained in WWTP-C and WWTP-D, operated by A2O and MBR processes, in which elimination of both poorly removed compounds and frequently detected compounds in influent slightly increased. It can be partially described by data of water quality, in which increased removal of organic pollutants and nitrogen sources was observed (WWTP-C). Also, MLSS concentration was 3 times higher than other WWTPs and it was operated by long SRT (WWTP-D), indicating that reduced PPCPs concentration in effluent can be related to high MLSS concentration in bioreactors.

3.3.3.2 Removal by post treatment after biological treatment

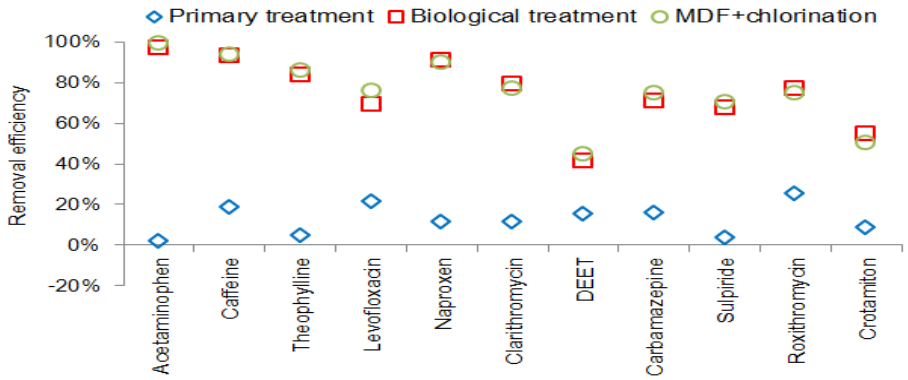
Most WWTPs employ various treatment processes to meet effluent regulations using disinfection and coagulation prior to discharge into receiving waters. These post treatment processes also can be applied efficiently to prevent adverse effects from the presence of PPCPs in the aquatic environment. Although many authors have focused on the study of treatment process for removal of PPCPs by adjusting experimental parameters like wavelength and contact time of ultraviolet (UV) or dosage of ozone, there are few studies on application of post treatment that has been used at current plants for both service of stable water quality and removal of PPCPs, and thus results on the removal by post treatment after biological treatment were evaluated.

As shown in Figure 3.7 (a), the combination of BFF and chlorination was used to limit activity of residual bacteria, in which the removal of sulfapyridine, atenolol and carbamazepine increased from 46%, 36% and 24% to 50%, 61% and 37%, respectively. This could be due to the effect of active surfaces within the BFF reactor that consisted of a matrix of microorganisms and extracellular polymers, allowing the attachment to solid surfaces (Hagopian et al., 1998). Also, Okuda et al. (2008) reported that chlorination could not remove pharmaceuticals sufficiently.

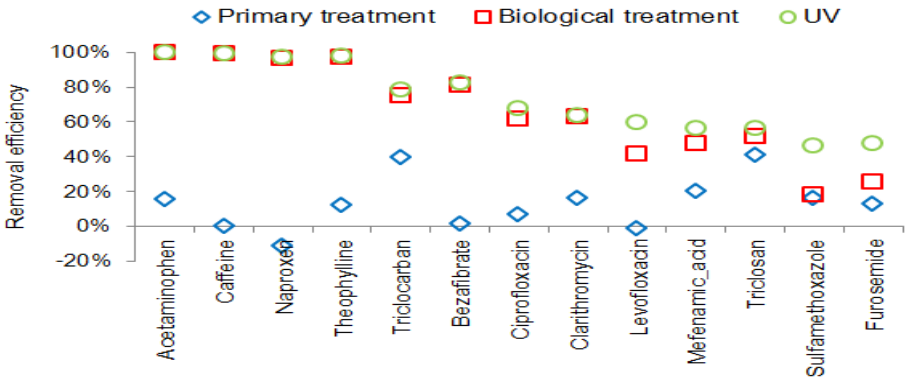
(a)


Primary treatment
Biological treatment
BFF+chlorination
Removal efficiency
100%
80%
60%
40%
20%
0%
Acetaminophen
Theophylline
Caffeine
Naproxen
Levofloxacin
Bezafibrate
Ciprofloxacin
Sulpiride
Clarithromycin
Sulfapyridine
Atenolol
Carbamazepine

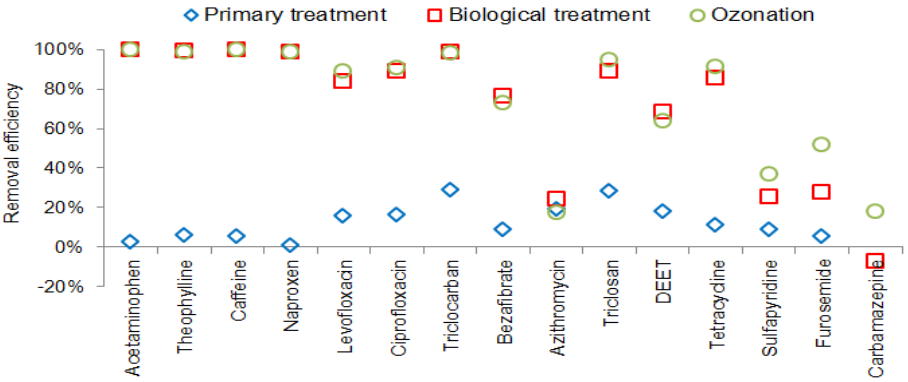
(b)


Primary treatment
Biological treatment
MDF+chlorination
Removal efficiency
100%
80%
60%
40%
20%
0%
-20%
Acetaminophen
Caffeine
Theophylline
Levofloxacin
Naproxen
Clarithromycin
DEET
Carbamazepine
Sulpiride
Roxithromycin
Crotamiton

(c)


Primary treatment
Biological treatment
UV
Removal efficiency
100%
80%
60%
40%
20%
0%
-20%
Acetaminophen
Caffeine
Naproxen
Theophylline
Triclocarban
Bezafibrate
Ciprofloxacin
Clarithromycin
Levofloxacin
Mefenamic_acid
Triclosan
Sulfamethoxazole
Furosemide

(d)


Primary treatment
Biological treatment
Ozonation
Removal efficiency
100%
80%
60%
40%
20%
0%
-20%
Acetaminophen
Theophylline
Caffeine
Naproxen
Levofloxacin
Ciprofloxacin
Triclocarban
Bezafibrate
Azithromycin
Triclosan
DEET
Tetracycline
Sulfapyridine
Furosemide
Carbamazepine

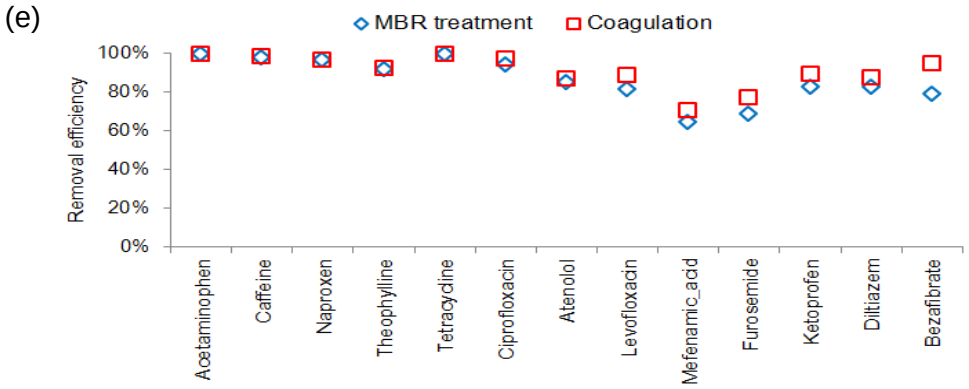


Figure 3.7 Removal by post treatment

(a) WWTP-A (D): biological fixed film (BFF) + chlorination, (b) WWTP-A (I): micro-media disk filters (MDF) + chlorination, (c) WWTP-B: UV treatment, (d) WWTP-C: ozonation and (e) WWTP-D: PAC coagulation

There was no significant difference between removal efficiency by biological treatment and post treatment in Figure 3.7 (b). It indicates that removal of PPCPs was not caused by chlorination disinfection and MDF. Its effective pore size was over 10 μm, while the size and molecular length of the PPCPs were much smaller than filter size and thus, disk filters was found to be less efficient for the removal of PPCPs.

Even though UV treatment is not very effective for removal of PPCPs at the doses normally applied for disinfection, the removal of some compounds like levofloxacin, mefenamic acid, sulfamethoxazole and furosemide slightly increased (Figure 3.7 (c)). Lam et al. (2004) demonstrated that levofloxacin and sulfamethoxazole were susceptible to direct and indirect photodegradation, which was in agreement with our study.

In addition to UV treatment, post treatment by ozone was investigated in Figure 3.7 (d). Ozone can accomplish great removal of various pharmaceuticals, but our research found most compounds were less well degraded except for furosemide, carbamazepine and sulfapyridine. Since post treatment by ozone at WWTP was only used as the purpose of disinfection, PPCPs and EDCs were not efficiently removed compared with existing reports (Kim et al., 2009). Recently, to improve the efficiency of ozonation ozone followed by activated carbon has been suggested as effective removal strategy because the ozone chemically degrades compounds and makes them more biodegradable, and then microorganisms living in the carbon bed can complete the degradation process (Lee., 2009).

In the case of MBR process, chemical coagulation treatment after membrane filtration is typically applied to reduce TP concentration of effluent (Figure 3.7 (e)). For the removal performance of some compounds such as diltiazem (5%), bezafibrate (16%),

ketoprofen (6%) and furosemide (8%), increased efficiencies were observed. However, it is difficult to interpret these results quantitatively, because the difference between residual concentration after membrane filtration and final effluent applied to coagulation was not significantly varied and their concentrations were not enough high to compare quantitative analysis (below 100 ng/L).

3.3.4 Removal characteristics of PPCPs in WWTPs

Removal characteristics of target compounds in wastewater are also important factors in assessing the performance of biological treatment systems. Although removal efficiency depends on the physico-chemical properties, characteristics of influent sources and operating conditions of WWTPs, biodegradation and adsorption are considered the most significant removal mechanisms of PPCPs removal during biological treatment. Therefore, to better understand their characteristics different WWTPs were investigated by comparing relationships between removal efficiency and k_d value, and the concept of evaluating the relationships was selected arbitrarily (Figure 3.8). Firstly, removal efficiency was classified into three groups: high removal (over 70%), moderate removal (ranged from 40% to 70%), and poor removal (below 40%). Secondly, the parameter known as the k_d value has been commonly used for adsorption studies in estimating distribution potential of contaminants present in aqueous solutions and thus, we used k_d values as parameters on adsorption tendency between target compounds and sludge of aerobic conditions (Eq.2.1)

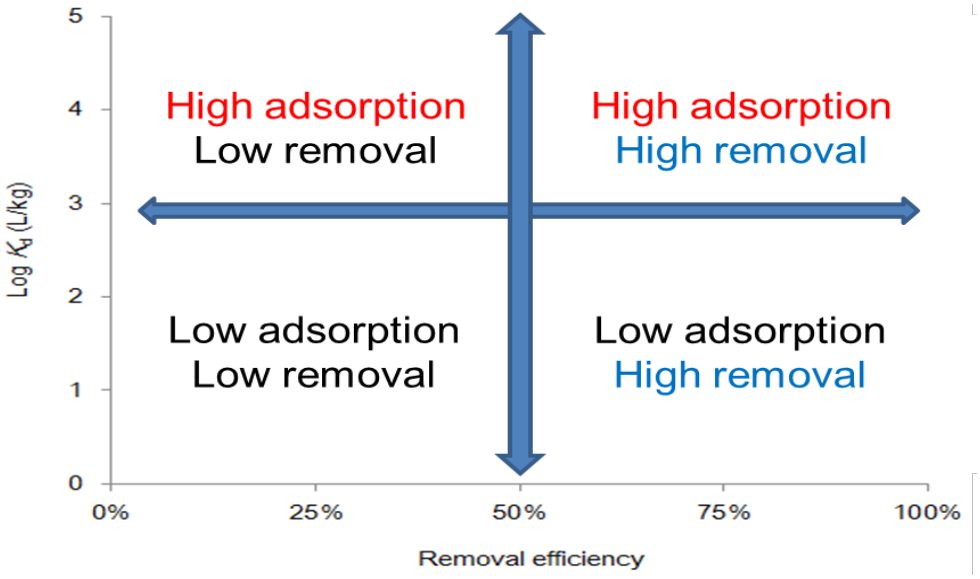
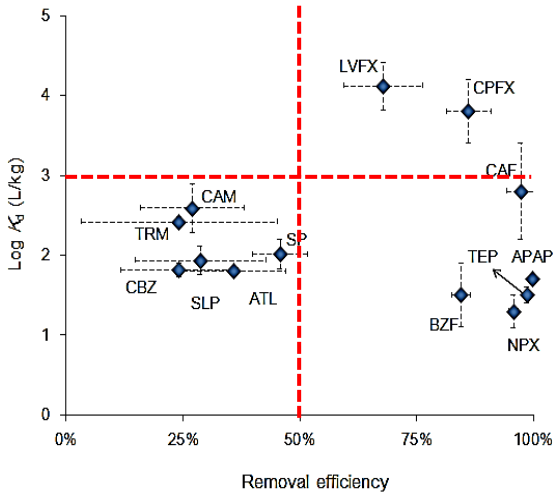
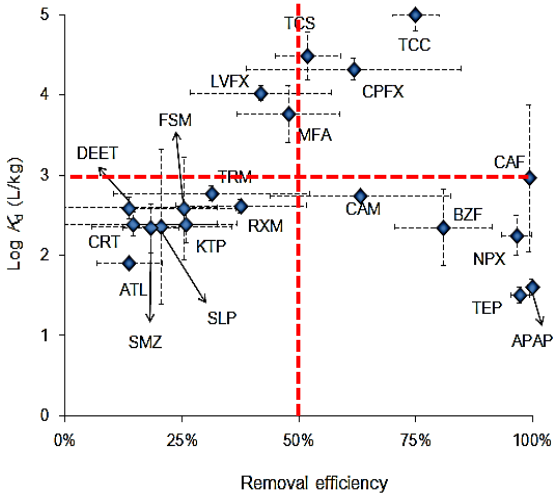


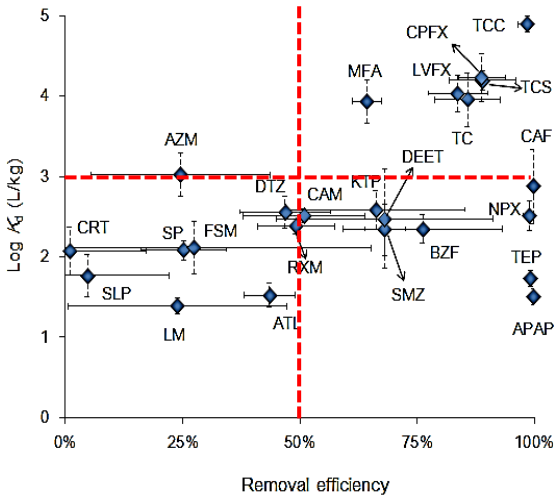
Figure 3.8 Relationships between Log K_d and removal efficiency



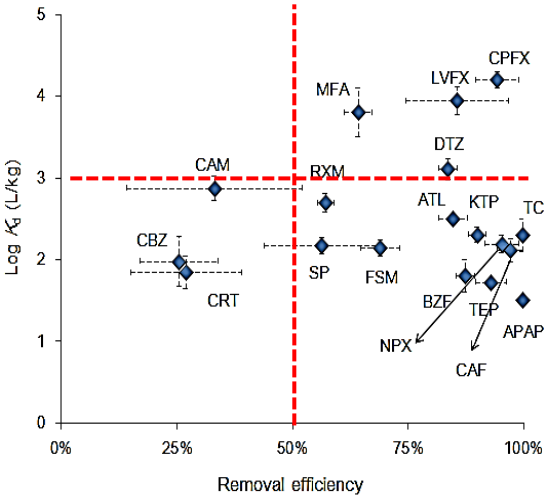
(a) WWTP-A (D)



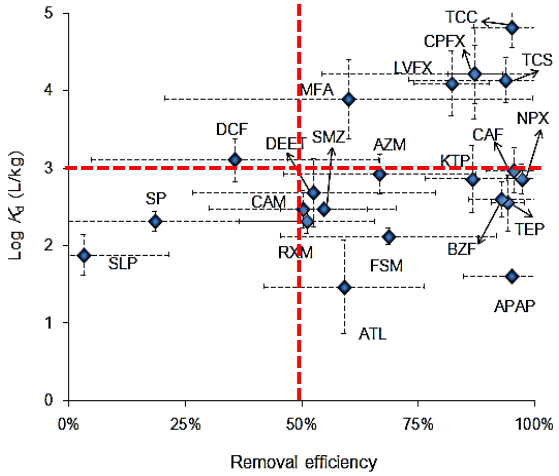
(b) WWTP-B



(c) WWTP-C



(d) WWTP-D



(e) lab-scale MBR

Figure 3.9 Removal characteristics of each WWTP and lab-scale study

Figure 3.9 shows the removal characteristics of each WWTP including lab-scale MBR study, in which individual compounds were scattered by removal efficiency and log K_d value. Both horizontal and vertical error bars were displayed by standard deviation. Some compounds which have been reported to show hydrophobic properties were not detected in both processes of WWTP-A due to the lower limit of quantification (LOQ). The level above which quantitative results may be obtained with a specified degree of confidence and the effects of low recovery rate, while great affinity for solid fraction was reported from the results of WWTP-B and WWTP-C. Particularly, triclocarban, triclosan, levofloxacin and ciprofloxacin showed high K_d values. Their values were compared to those reported by Narumiya et al. (2013) and Kim et al. (2014), indicating that log K_d values ranging from 4.0 to 5.1 for target compounds had strong potential on adsorption onto sludge. Removal efficiency of PPCPs that were characterized by hydrophilic properties with very low log K_{ow} was much higher than that of other compounds in all surveyed WWTPs (e.g., acetaminophen, caffeine, theophylline and naproxen), but their K_d values were found to be less than log 3, which means that their removal was not strongly related to effect of adsorption. As can be shown in Figure 3.9, PPCPs showing poor and moderate removal as well as K_d values with below log 3 were not greatly eliminated in WWTP-A (D), WWTP-B, and WWTP-C, whereas lab-scale MBR appeared to be effective in removing these compounds except for sulfapyridine and sulpiride. Similarly, even though increase of removal efficiency was apparently achieved, fluctuations of K_d values were not observed. For instance, removal efficiency of ketoprofen, furosemide and atenolol were 26, 25 and 14% in WWTP-B and 66, 28, 44% in WWTP-C, whereas their removals reached to 90, 69 and 85% in WWTP-D and 87, 69 and 59% in lab-scale MBR. Given that adsorption affinity was not significantly varied, increased removal performance of these compounds can be attributed to enhanced biodegradation potential in MBR process rather than adsorption to sludge.

Among the studied WWTPs, our concept on correlations between removal performance and adsorption tendency was well identified in WWTP-C and thus the result of this plant was compared to lab-scale MBR process to evaluate removal characteristics of each process. Classification on degree of removal and adsorption tendency of PPCPS are represented in Table 3.6 in details. For both poorly and no removed compounds in WWTP-C, overall removal efficiency increased in lab-scale MBR. Some compounds such as bezafibrate and diltiazem showed slightly improved removal efficiency. In contrast, though a high adsorption tendency was observed in K_d values with 4.9, 4.2, 4.2, 4.0, 3.9 and 4.0 in WWTP-C and 4.8, 4.1, 4.2, 4.1, 3.9 and 4.2 in lab-scale MBR for triclocarban, triclosan, ciprofloxacin, levofloxacin, mefenamic acid

and tetracycline, respectively, no further increase was observed in the conditions of high MLSS concentration (around 8,000 mg/L) developed in lab-scale MBR. It was apparent that considering the contribution of adsorption in removal of high adsorptive compounds cannot be possible from adsorption capacity based on the K_d values.

Table 3.6 Degree of removal and log k_d value of PPCPs

Degree of removal	**High removal (> 70%)**		**Moderate removal (40-70%)**		**Poor removal (< 40%)**		**Log K_d value (> 3)**	
WWTP-A (D) - Symbio	APAP TEP CAF	NPX BZF CPFX	LVFX SP		SLP DEET CAM ATL TRM	SMZ CRT CBZ RXM	LVFX CPFX	
WWTP-A (I) - Symbio	APAP CAF TEP NPX	CAM CBZ CRT	LVFX SLP CRT		DEET FSM		LVFX	
WWTP-B - 5-stage BNR	APAP CAF NPX	TEP TCC MFA	CPFX CAM LVFX TCS MFA		ATL SLP RXM DEET SMZ TRM	KTP SP CRT LM FSM CBZ	CPFX LVFX TCC MFA TCS TC	
WWTP-C - A2O	APAP TEP CAF NPX LVFX	CPFX TCC BZF TCS TC	CAM ATL MFA RXM	KTP SMZ DEET DTZ	SP AZM SLP FSM	LM CBZ DCF	LVFX CPFX TCC MFA	AZM TCS TC
WWTP-D - MBR	APAP CAF NPX TEP TC	ATL LVFX KTP DTZ BZF	MFA SP FSM RXM		SLP DEET CAM	CBZ DCF CRT	CPFX LVFX MFA DTZ	
Lab-scale MBR	APAP CAF NPX TEP BZF CPFX	LVFX TCC KTP LM TC TCS	CAM ATL MFA RXM AZM	FSM SMZ DEET DTZ	SLP SP DCF	CBZ CRT RTM	LVFX CPFX TCC MFA	DCF TC TCS

3.3.5 Comparison of removal mechanisms

Removal characteristics of PPCPs have been discussed in chapter 3.3.4, but it was not clearly explained that adsorption tendency was deeply related to the k_d values. That is, their values could describe the fraction of the target compounds adsorbed to sludge,

but it was hard to take into account the adsorbed PPCPs concentration during wastewater treatment process, particularly biological treatment because of different sludge properties and the effect on operating conditions of reactor such as HRT and SRT. Thus, removal mechanisms were evaluated to understand the fate of detected compounds through calculations of mass balance.

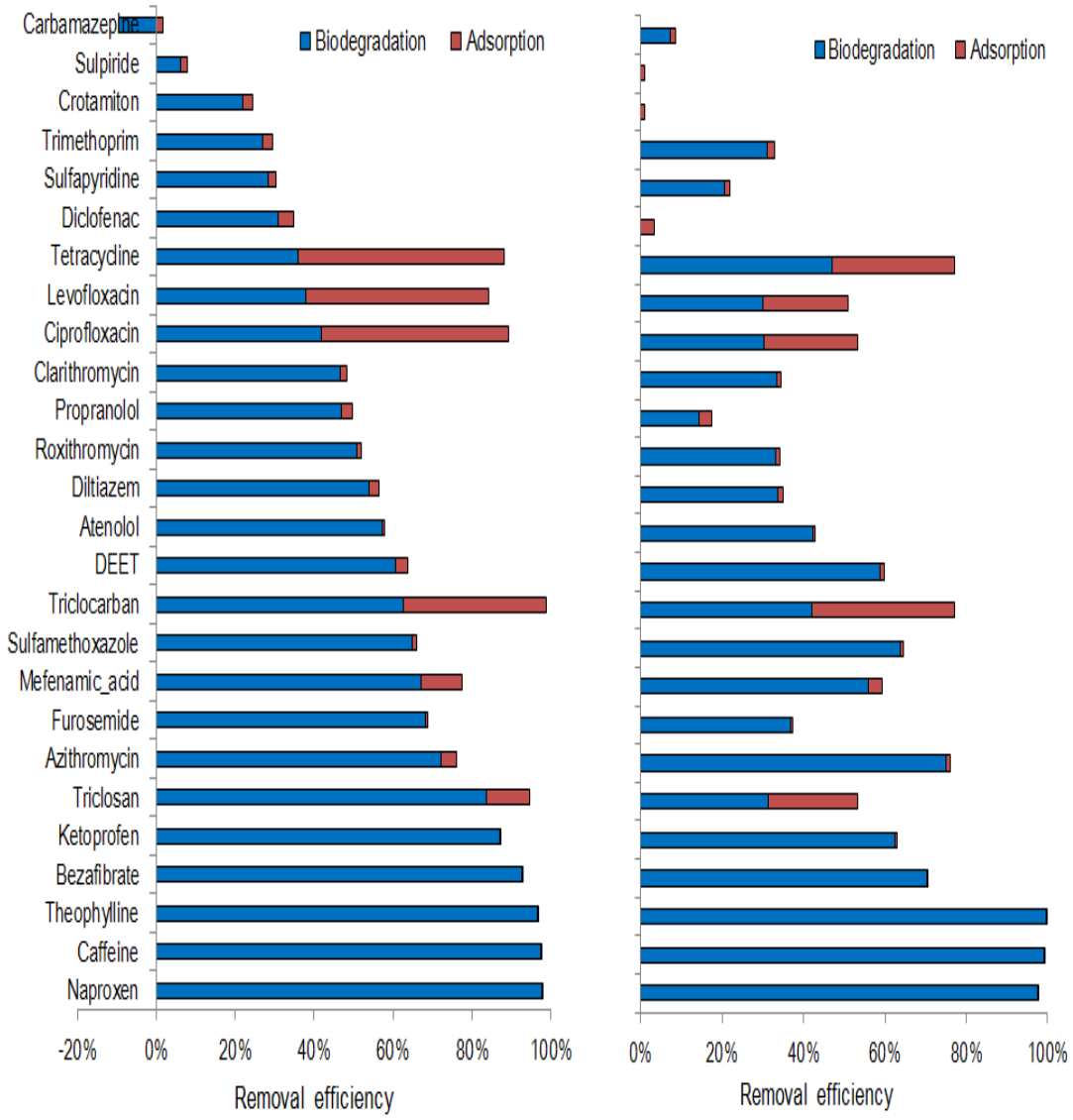


Figure 3.10 Mass balance of lab-scale MBR (left) and A2O process (WWTP-C, right)

Moreover, the role of biodegradation and adsorption in the removal of pharmaceutically active compounds with different bulk organic matter characteristics was studied. As can be seen in Figure 3.10, mass balance of WWTP-C was compared to that of lab-scale MBR process. To estimate removal pathways during

only biological treatment, removal by primary clarifier of WWTP-C was not considered and comparative evaluation was conducted using the same influent sources. Appropriate surrogate standards were used for the quantification of the samples and the data are represented in Table 3.7.

Table. 3.7 Recovery rate of solid phase samples

Compounds	Lab-scale MBR						WWTP-C (A2O process)					
	Anoxic (n=11)			Aerobic (n=11)			Aerobic (n=7)			Sec.sludge (n=7)		
	Freq.	Avg.	SD	Freq.	Avg.	SD	Freq.	Avg.	SD	Freq.	Avg.	SD
Sulpiride	-	-	-	-	-	-	-	-	-	-	-	-
Salbutamol	2	36%	13%	1	41%	14%	2	70%	26%	3	51%	27%
Atenolol	2	37%	12%	1	40%	13%	6	43%	20%	4	52%	21%
Acetaminophen	5	51%	22%	5	82%	24%	2	36%	24%	5	71%	21%
Sulfathiazole	11	79%	24%	10	84%	35%	6	71%	22%	5	86%	22%
Theophylline	11	98%	25%	10	100%	27%	7	100%	27%	5	87%	13%
Sulfapyridine	11	94%	28%	10	95%	19%	6	97%	26%	5	91%	14%
Sulfamerazine	11	97%	25%	10	97%	19%	6	99%	23%	6	91%	21%
Thiamphenicol	11	79%	24%	10	84%	25%	3	71%	32%	6	86%	16%
Caffeine	11	118%	15%	10	118%	15%	7	105%	15%	4	89%	16%
Trimethoprim	11	118%	15%	10	118%	15%	4	105%	15%	6	89%	16%
Lincomycin	-	-	-	-	-	-	-	-	-	-	-	-
Levofloxacin	7	42%	19%	7	44%	21%	5	62%	20%	7	75%	22%
Norfloxacin	2	58%	21%	3	53%	24%	6	56%	32%	7	72%	20%
Sulfadimidine	6	97%	32%	5	80%	59%	5	86%	15%	6	82%	10%
Pirenzepine	11	118%	15%	10	118%	15%	4	105%	15%	5	89%	16%
Tetracycline	4	47%	21%	3	52%	21%	3	87%	23%	4	88%	26%
Ciprofloxacin	2	61%	22%	3	51%	22%	4	60%	33%	3	74%	15%
Oxytetracycline	4	47%	21%	3	52%	21%	4	87%	53%	4	88%	25%
Sulfamethoxazole	11	90%	21%	10	95%	19%	4	99%	31%	5	96%	35%
Sulfamonomethoxine	11	97%	25%	10	97%	29%	7	99%	23%	7	91%	21%
2QOA	11	79%	29%	10	86%	21%	3	63%	21%	7	79%	21%
Enrofloxacin	2	61%	22%	3	51%	22%	4	60%	13%	3	74%	14%
Antipyrine	11	107%	15%	10	106%	12%	4	102%	16%	6	101%	11%
Clenbuterol	11	106%	13%	10	105%	14%	6	112%	14%	5	115%	16%
Primidone	11	93%	25%	10	97%	29%	6	78%	24%	6	87%	30%
Metoprolol	11	106%	11%	10	104%	11%	4	101%	20%	5	102%	22%
Disopyramide	9	100%	28%	7	98%	38%	5	91%	25%	4	98%	27%
Ethenzamide	-	-	-	-	-	-	-	-	-	-	-	-
Sulfadimethoxine	10	76%	29%	10	85%	29%	6	90%	25%	7	82%	22%
Cyclophosphamide	11	100%	17%	10	99%	19%	6	95%	22%	7	86%	14%
Ifenprodil	11	102%	11%	10	103%	10%	5	100%	21%	7	106%	16%
Azithromycin	9	73%	26%	7	75%	25%	2	59%	24%	4	49%	11%
Propranolol	9	100%	28%	7	98%	38%	4	91%	25%	7	98%	27%
Furosemide	11	91%	26%	9	91%	37%	5	93%	25%	5	81%	14%
Diltiazem	11	102%	11%	10	103%	10%	7	100%	21%	7	106%	16%
Carbamazepine	10	111%	22%	10	116%	19%	7	105%	20%	7	96%	20%
Isopropylantipyrine	11	107%	15%	10	106%	12%	7	102%	16%	7	101%	11%
Tiamulin	11	102%	11%	10	103%	10%	6	100%	21%	7	106%	16%
Dipyridamole	11	82%	22%	10	83%	21%	6	103%	35%	4	110%	15%
Tylosin	11	102%	11%	10	103%	10%	6	100%	21%	5	106%	16%
Griseofulvin	11	125%	14%	10	128%	12%	6	119%	10%	5	111%	6%
DEET	11	88%	17%	10	92%	8%	6	89%	23%	5	84%	6%
Clofibric_acid	10	109%	36%	10	107%	17%	6	107%	17%	7	103%	13%
Ketoprofen	11	125%	14%	10	128%	12%	6	119%	10%	7	111%	6%
Clarithromycin	11	120%	22%	10	117%	21%	6	104%	27%	7	108%	18%
Naproxen	11	125%	14%	10	128%	12%	4	119%	10%	7	111%	6%
Roxithromycin	8	127%	28%	7	124%	24%	5	98%	21%	6	108%	19%
Crotamiton	10	75%	21%	10	76%	12%	6	77%	20%	5	70%	10%
Bezafibrate	7	123%	20%	7	125%	21%	4	105%	29%	7	108%	25%
Fenoprofen	11	125%	14%	10	128%	12%	5	119%	10%	3	111%	6%
Diclofenac	10	77%	30%	10	76%	28%	5	83%	28%	5	76%	20%
Indometacin	10	94%	34%	10	91%	29%	5	103%	32%	6	94%	17%
Triclosan	1	57%	17%	1	34%	12%	2	55%	14%	2	58%	13%
Mefenamic_acid	5	55%	23%	6	49%	21%	4	74%	27%	6	71%	27%
Chlortetracycline	4	47%	21%	3	52%	21%	3	87%	13%	2	88%	26%
Triclocarban	1	51%	15%	2	36%	14%	3	71%	12%	2	82%	25%

As remarked in analytical methods (chapter 3.2.2), samples of solid phase were extracted by organic solvents with pH control. Even though the recovery rate was low in comparison with that of liquid samples, it ranged from 30% to 130% except for the compounds that were analyzed without surrogate standards, which were consistent with previous reported study by Narumiya et al. (2013). From the results of recovery data it demonstrates that pretreatment and analysis used in this study were regarded as appropriate methods.

For the results of mass balance, frequently detected compounds in influent like naproxen, caffeine and theophylline were efficiently removed by biodegradation regardless of treatment types (over 97%) and removal by adsorption was not observed due to their hydrophilic characteristics. Bezafibrate, ketoprofen, and furosemide were moderately removed in A2O process, with the average removal efficiency of 70%, 63%, and 37%, respectively, and their removal performance increased up to 93%, 87%, and 68% in lab-scale MBR process, while removal by adsorption showed less than 1% in these compounds. Enhanced removal efficiency in lab-scale MBR was similar to the results of other studies (Radjenovic et al., 2007; Radjenovic et al., 2009; Kasprzyk-Hordern et al., 2009).

Removal efficiency of beta blockers and antiarrhythmic agents like atenolol (42% -> 57%), propranolol (14% -> 47%) and diltiazem (34% -> 54%) was higher in lab-scale MBR compared with A2O process, in which the ratio of removal by adsorption to overall removal was below 4%, while removal by adsorption was partially achieved in A2O process. According to Maurer et al. (2007), faster biodegradation of beta blocker was achieved by MBR sludge, whereas adsorption was identified as possible removal pathway only for propranolol, which was in good agreement with our research.

The similar tendency was shown in macrolide antibiotics. Roxithromycin and clarithromycin were attenuated up to 33% and 34% in A2O process, whereas in lab-scale MBR removal performance slightly increased (51% and 46%). The low removal of these compounds in CAS system has been reported by several authors. For instance, the reported removal ranged from -20% to 66% in roxithromycin and from 9% to 21% in clarithromycin, while increase of removal performance was obtained in MBR process (Sahar et al., 2011; Kazama., 2014). Kimura et al. (2007) has reported that sludge of CAS and MBR have large specific sorption capacities that can be attributed to the high specific surface area of the suspended microbial population. However, recent studies have indicated that the removal of many PPCPs by the MBR process is mainly due to biodegradation. This is because the low concentration of TOC in a slow growing culture with long SRT can allow organisms to develop degradation pathways for slowly

degradable compounds in order to continue to recover energy to support microbial growth (Lee., 2009).

For five compounds such as triclosan, triclocarban (antibiotics), ciprofloxacin, levofloxacin (fluoroquinolone antibacterials) and tetracycline, total removal performance including biodegradation and adsorption was greater in lab-scale MBR than A2O process. In addition to elimination of PPCPs by biodegradation, lab-scale MBR slightly enhanced their elimination by adsorption to around 10% except for triclosan which showed higher adsorption tendency in A2O process, but total removal efficiency was higher in lab-scale MBR process (around 95%), suggesting that higher MLSS concentration as well as better capability of microorganisms to adsorb target compounds contributed to a greater increase in adsorption. In particular, previous studies have proved that ciprofloxacin and tetracycline have low log K_{ow}, thereby resulting in the elimination by biodegradation. However, our results showed that they have a high tendency to adsorb to sludge (high K_d value) in both processes, and thus this may be related with a previous study that demonstrated the adsorption tendency of ciprofloxacin and tetracycline was originated from electrostatic forces and not hydrophobic interactions (Li et al., 2010).

To sum up, overall removal performance was higher in lab-scale MBR than in A2O process due to high MLSS concentration of MBR sludge. With regard to similar K_d value between lab-scale MBR and A2O process, no significant differences were observed, but comparative evaluation by mass balance demonstrated that adsorption tendency of some compounds was enhanced in lab-scale study. However, the removal originated from biodegradation also increased. Therefore, when compared to A2O process, the higher removal efficiency found in lab-scale MBR was primarily affected by biodegradation. Biodegradation was found to be the main removal pathway for eliminating PPCPs, whereas adsorption appeared to be a minor mechanism with the exception of high adsorptive compounds.

3.4 Conclusions

The occurrence and fate of 57 PPCPs were studied in MBR process, with each unit of different WWTPs to evaluate removal characteristics of these compounds. Furthermore, this study focused on comparison of the removal characteristics between lab-scale MBR and A2O process by classifying them and by calculating mass balance. The findings are as follows:

1) The fourth most detected compounds in all studied influent samples were acetaminophen, caffeine, naproxen and theophylline. Particularly, in the aspects of category of compounds, analgesics and antibiotics were observed at the highest level, and their mass loading rate including stimulant, NSAIDs, and antibacterials accounted for median 85% of all WWTPs. Also, there were no significant differences between total per capita loads of the surveyed WWTPs, excluding WWTP-A (I). Over 92% of PPCPs in influent were eliminated in our study, which was comparable to WWTPs of other countries.

2) For all studied WWTPs, better removal was obtained in WWTP-C and WWTP-D, operated by A2O and MBR processes, in which elimination of not only poorly removed compounds, but also frequently detected compounds in influent was found to be efficiently achieved. For UV and ozone treatment, although removal of PPCPs under the conditions normally applied for disinfection was not achieved, the removal of levofloxacin, mefenamic acid, sulfamethoxazole and furosemide in UV treatment and furosemide, carbamazepine and sulfapyridine in ozone treatment slightly increased.

3) Removal characteristics were evaluated by degree of removal and K_d value of target compounds, showing that for both poorly eliminated compounds and K_d values with below log 3 in WWTP-A (D), WWTP-B and WWTP-C, overall removal efficiency increased in lab-scale MBR (e.g., bezafibrate, ketoprofen and atenolol) However, regarding these compounds, there was no significant difference on their K_d values between various biological treatment processes and MBR process.

4) To better understand removal characteristics of lab-scale MBR and A2O process mass balance was calculated, indicating that increased removal performance found in lab-scale MBR was attributed to enhanced biodegradation and adsorption tendency, in which the main removal route was found to be biodegradation, while adsorption was deemed to be a minor pathway except for some compounds with high adsorptive characteristics.

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ChapterⅣ

Fouling Reduction and Biodegradability Enhancement of PPCPs by Coagulation-MBR

4.1 Introduction

Several studies have reported the advantages of MBR process over conventional biological wastewater treatment because this technology is able to generate less sludge rate and produce better water quality whilst possessing small footprint and relatively low capital and operating costs (Adham et al., 2001; Judd et al., 2011). Also, application of MBR process for dealing with the treatment of emerging contaminants is increasingly the focus of international attention. As mentioned in Chapter III, it has been proven by our study that MBR process was superior to other biological treatment processes in removal of many target compounds.

However, the extensive application of MBR process is still limited due to the frequent regeneration including both of physical and chemical cleaning which causes the increased maintenance costs, flux decline and membrane fouling (Le-Clech et al., 2006). In particular, membrane fouling can give rise to severe flux decline and affect produced water quality, which is a major obstacle to the widespread use of this system. In order to address these problems, various methods have been investigated by controlling critical flux, applying effective backwash and supplying air micro-bubbles (Wang et al., 2008; Hwang et al., 2009; Hosseinzadeh et al., 2013).

Another great way to control membrane fouling is to lower the fouling potential in the mixed liquor using effective chemical additives. Although coagulation treatment forms an integral part of the conventional water treatment scheme and have been applied at downstream of biological treatment process to decrease turbidity and meet phosphorus concentration of effluent, it has been reported that coagulant dosing into MBR process

assist greatly in reducing the TMP of reactor and thereby result in improvement of permeate flux and a prolonged operation (Hai et al., 2007; Koseoglu et al., 2008; Matilainen et al., 2010; Chen et al., 2012).

On the other hand, coagulation is not regarded as the effective method with regard to removal of PPCPs and thus advanced treatment such as AOP and NF/RO filtration can be used to eliminate these compounds. However, since the advanced processes are more energy intensive and complex in operation than conventional treatment processes (Alexander et al., 2012) they have not been considerably implemented in WWTP. Even though coagulation treatment has been found to be inefficient in eliminating PPCPs and the existing process has not been designed for the purpose of PPCPs removal, there have been only a few studies on removal fate and performance of PPCPs in the combination of MBR with coagulation.

The aim of Chapter IV, therefore, was to evaluate fouling control and permeation properties by coagulation and investigate removal performance of PPCPs in coagulation-MBR with types and dosages of additives. Furthermore, the study on whether it is effective for long-term operation was conducted by comparing control-MBR and coagulation-MBR. This study will give useful insights into the applicability of processes combining physicochemical and biological treatments in terms of the removal of PPCPs.

4.2 Materials and methods

4.2.1 Experimental design

The experiment in this study was divided into three stages and the summary of experimental conditions including operational period, types of the experiments, dosage and pH is represented in Table 4.1.

The first stage of experiment was the selection of optimal parameters. Two coagulants (chitosan and PAC) were evaluated to investigate the variations of sludge properties and fouling resistance. MBR used in lab-scale study of Chapter III was employed and two reactors were operated in parallel to compare the effect of two coagulants. With a few exceptions (experimental conditions in stage 1), their specification and operating parameter were the same to the previous research. In this

Table 4.1 Summary of experimental conditions

	R1	R2
Stage 1	**Experimental period: Sep, 2014 – Dec, 2014 (continuous operation)**	
Coagulant	PAC	Chitosan
Dose	From 0 to 50 mg/L	From 0 to 20 mg/L
pH	-	-
Stage 2	**Experimental period: Dec, 2014 – Feb, 2015 (batch experiments)**	
Coagulant	PAC	Chitosan
Dose	From 0 to 50 mg/L	From 0 to 20 mg/L
pH	From 5 to 9	From 5 to 9
Stage 3	**Experimental period: Feb, 2015 – Jun, 2015 (continuous operation)**	
Coagulant	PAC (coagulation-MBR)	Control (control-MBR)
Dose	20 mg/L	-
pH	-	-

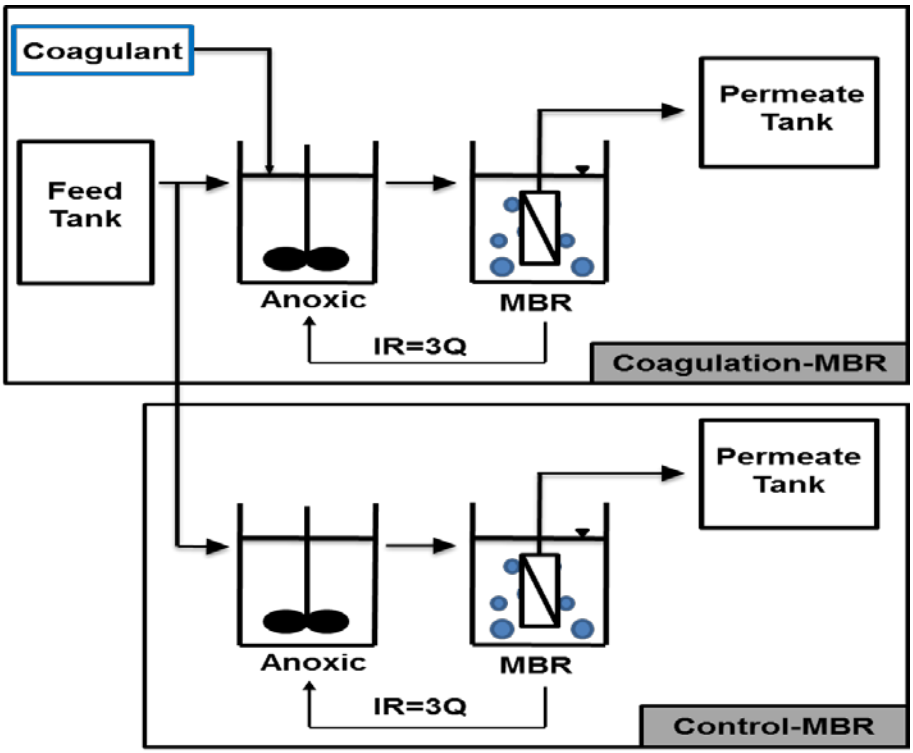


Figure 4.1 Schematic diagrams of coagulation-MBR and control-MBR in stage 3

stage, the influence of coagulant types and dosages was determined.

Batch experiments were conducted in the second stage, in which removal of PPCPs was investigated in terms of types of coagulants, dosage and pH. Dosages of 1, 5, 10, 20, 50 mg/L in PAC or 1, 2, 5, 10, 20 mg/L in chitosan were studied, respectively. The pH ranged from 5 to 9 in both conditions.

Lastly, the third stage was performed from the results of stage 1 and 2. The schematic of the experiments is shown in Figure 4.1. The same influent was fed into the both coagulation-MBR and control-MBR, whereas selected coagulant was only pumped to coagulation-MBR by the dosing pumps, herein, the operation was continued during 4 months. In this stage, removal characteristics of coagulation-MBR and applicability of this process for long-term operation was evaluated.

4.2.2 Preparation of coagulants

Two different types of coagulants like inorganic (PAC) and organic (chitosan) were tested in this study. These coagulants were purchased from chemical company, Korea and they were currently being used in the field of wastewater treatment. Stock solution of PAC was prepared by dissolving commercial grade PAC (18% of Al_2O_3, 36-42% of basicity) in distilled water. Also, because chitosan is able to maintain soluble state in acidic condition (below pH 6) it was mixed with 10 ml of 0.1M HCl solution for 10 hours to dissolve the powder.

4.2.3 Critical flux and backwashing

The original definition of critical flux is the maximum flux obtainable without deposition of foulants on the membrane surface (Yoon., 2015). Although membrane is fouled at a low rate in any flux, a sustainable flux can maintain long-term operation in submerged membrane bioreactors before the TMP reaches an unacceptable level (Zhang et al., 2006). A flux-step method has been developed for evaluating fouling in MBR process operating at constant flux (Le-Clech et al., 2003). In this study, critical flux was determined by measuring key parameters such as flux and TMP, in which change of TMP with time at each flux was monitored. Specifically, in the beginning, a low flux was fixed for 5 to 15 min under regular filtration conditions and operation was stopped for 1 to 5 min to relax the membrane. The flux-TMP profile was continuously monitored until TMP increased distinctively faster than in the previous step. The highest flux which cannot cause a significant rise or jump of TMP during the operation cycle was

determined as a critical flux (Yoon., 2015).

Maintenance cleaning using sodium hypochlorite (NaOCl) with the effective choline concentration of 300 to 1,000 mg/L is intended to remove fouling on membrane surface regularly to inhibit the thickening of the cake layer and a rise in TMP for stable operation. If TMP is still high after cleaning by NaOCl, clogging is considered to have been caused by inorganic matter, thereby performing backwashing in place by acid (oxalic acid: 1%, citric acid: 1%, sulfuric acid or hydrochloric acid: 0.1 to 0.5 N).

4.2.4 Analytical methods

4.2.4.1 Analysis of particle size and zeta potential

Analysis of particle size and zeta potential was simultaneously measured by analytical instrument (Malvern, Zetasizer Nano series) which incorporates combinations of a particle size and zeta potential analyzer. The particle size distribution by laser diffraction was based on the principle that particles passing through a laser beam will scatter light an angle that is directly related to angles, thus particles ranged from 0.3 nm to 10 μm could be precisely monitored in this study. The zeta potential of the sludge particles in the supernatant was determined using measurement principle, electrophoretic light scattering. Both were used to investigate the variations of sludge properties in adding coagulants under studied conditions.

4.2.4.2 Permeability resistance

The resistance in series model has been adapted to account for the influence of membrane fouling (Blanpain et al., 1997; Gésan-Guisiou et al., 1999; Choi et al., 2005; Brião et al., 2012). The relation between TMP and permeate flux can be expressed using this model. In MBR process, cake layer can be formed on membrane surface when the process is operated continuously without effective backwashing and thus, the permeation properties and hydraulic resistance were evaluated according to Darcy's law by Eq.4.1. Also, to understand which resistance component is dominant specific resistance was calculated by Eq.4.2.

$$J = \frac{\mathrm{V}d}{\mathrm{A}d\mathrm{t}} = \frac{\Delta \mathrm{P}}{\mu \cdot R_{\mathrm{t}}} \qquad \text{(Eq.4.1)}$$

$$R_t = R_m + R_f + R_c \quad \text{(Eq.4.2)}$$

Where,

J: Permeate flux ($m^3/m^2/s$ or m/s)
A: Effective membrane surface (m^2)
V: Permeate volume (m^3)
ΔP: TMP (Pa, $kg/m/s^2$)
μ: Viscosity of permeate (kg/m/s or cP, $1.00x10^{-3}$ kg/m/s for water at 20 ℃)
R_t: Total membrane resistance (m^{-1})
R_m: Intrinsic resistance of new membrane (m^{-1})
R_f: Irreversible fouling resistance (m^{-1})
R_c: Cake resistance (m^{-1})

4.2.4.3 Extraction of extracellular polymeric substances (EPS) and soluble microbial products (SMP)

Membrane fouling is a complicated phenomenon caused by interactions between the membrane material and the components in the activated sludge, essentially being the EPS. Microbial EPS are high molecular-weight mucous secretions from microbial cells. They can play an important role for floc formation in activated sludge liquors (Sanin et al., 2000; Liao et al., 2001). The EPS matrix is very heterogeneous, with polymeric materials including polysaccharides, proteins, lipids, and nucleic acids (Bura et al. 1998; Nielson et al., 1999).

In this study, modified steaming extraction method by Brown was used to extract bound and soluble EPS (Brown et al., 1980; Sperandio et al., 2005). The protein content of EPS was determined by Lowry method with bovine serum albumin (BSA) as the standard. In brief, 10 ml of samples were collected from the mixed liquor and centrifuged with 3,500 rpm for 10 min, in which concentrated sludge was suspended again by 0.9% NaCl after the supernatants were removed. The samples were extracted repetitively and then processed by heating (90±3 ℃) during 1 hr. Finally, the concentrations of all samples for protein were measured using a UV spectrophotometer at wavelength of 660 nm. Also, polysaccharide amount was assessed using phenol-sulphuric acid method, with glucose as the standard (Lowry et al., 1951; Dubois et al., 1956). 100 ml samples were prepared by addition of 500 ml of 5% (w/v) liquid

phenol solution and 2.5 ml of concentrated sulfuric acid. The calculation of EPS was based on the following equations:

$$\mathrm{EPS}\ (\mathrm{mg/g_{VSS}}) = \frac{(\mathrm{Protein} + \mathrm{carbohydrate})}{\mathrm{VSS}} \qquad \text{(Eq.4.3)}$$

For the analysis of SMP, 100 ml of the activated sludge was collected from MBR process and allowed to settle for 1hr at 4 ℃. After the supernatant was decanted, the sludge was centrifuged with 3,500 rpm for 15 min. And then, the supernatant was prepared as SMP of the sludge flocs.

4.2.4.4 Membrane filtration test

Dead-end stirred cell (Millipore amicon, 8200) was used to characterize membrane filtration and their separation behavior. This experiment was conducted with membrane having effective area of 28.7 cm^2 and diameter of 63.5 mm, and schematic diagram of the experiment are represented in Figure 4.2. The feed that was collected in solution reservoir was supplied by nitrogen gas with constant rate of 55 psi to head space of stirred cell device. The gentle magnetic stirrer was employed to minimize concentration polarization and shear denaturation. Permeate volume was monitored using automatic balance.

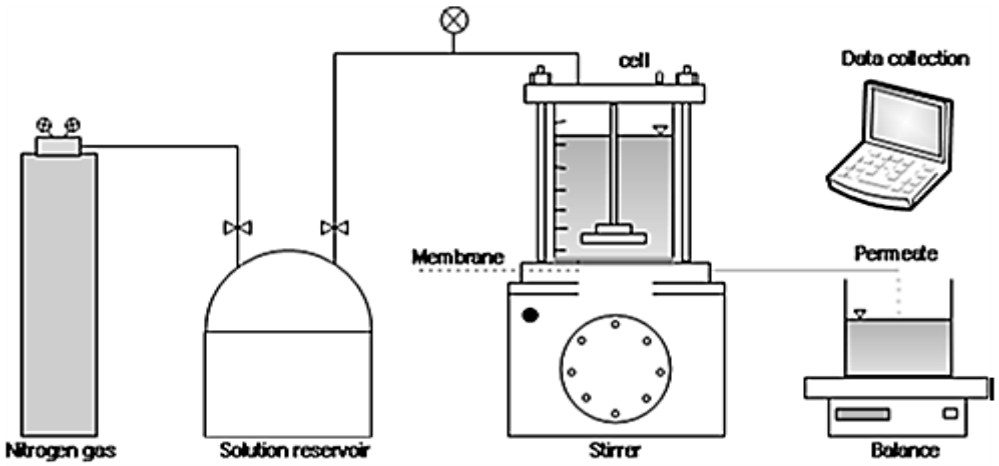


Figure 4.2 Schematic diagram of filtration experiment

4.2.4.5 Analysis of scanning electron microscope (SEM) and energy dispersive X-ray (EDX)

SEM was used to analyze morphology and cross section of membrane surface and cake layer. Element analysis of organic and inorganic foulants on membrane surface was conducted simultaneously through analysis of EDX. The EDX is an analytical technique used for the elemental experiment and chemical characteristics of sample. Also, it makes use of the X-ray spectrum emitted by sample bombarded with a focused beam of electrons to obtain a localized chemical analysis.

As the purpose of pretreatment, coating of samples was carried out to improve the imaging of the samples by applying an ultra-thin coating of electrically-conducting metal such as gold (Au) and silver (Ag). After the pretreatment was successfully completed, coated samples were analyzed by analytical instrument (Hitachi, S-3400N) which is shown in Figure 4.3.

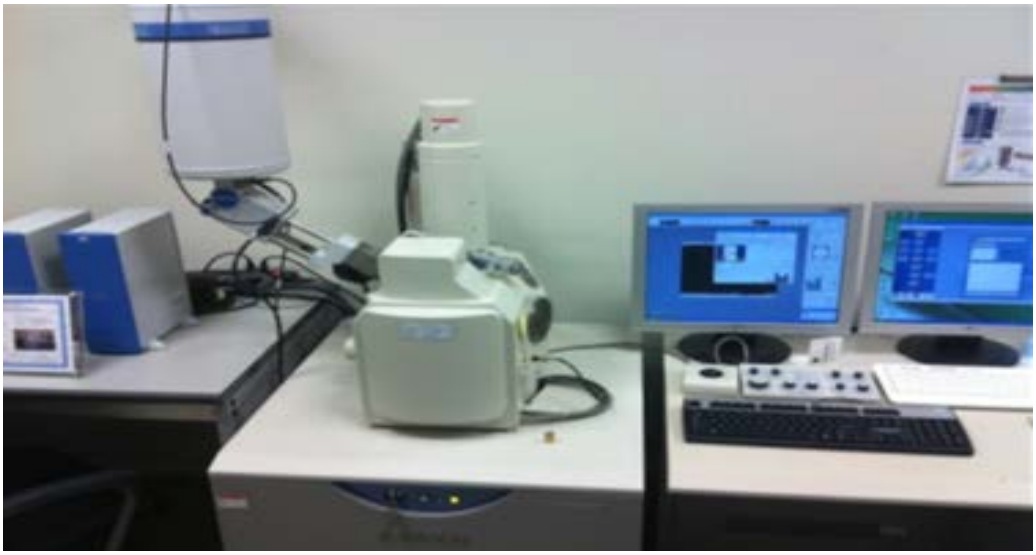


Figure 4.3 Analytical instrument of SEM/EDX

4.3 Results and discussion

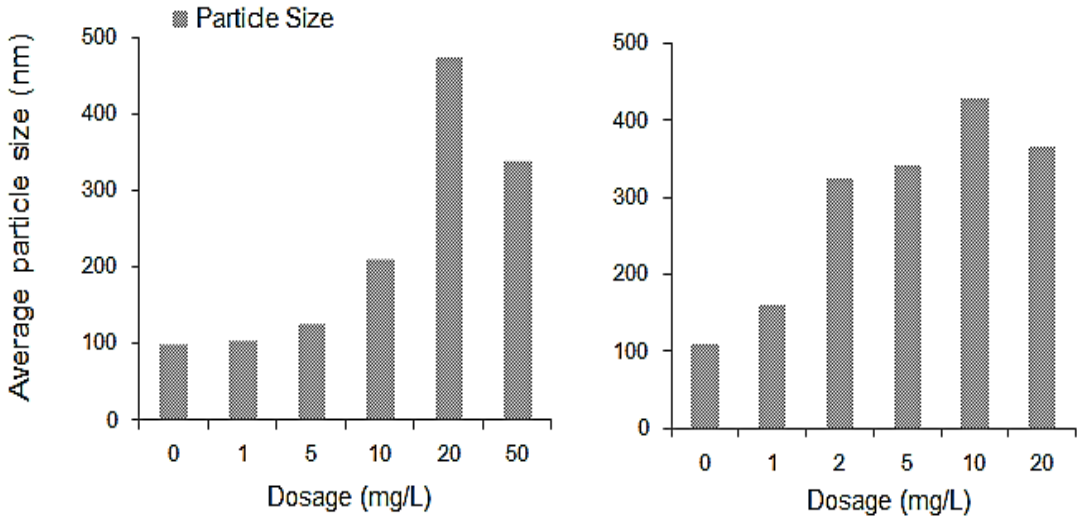
4.3.1 Variations of sludge properties by coagulation

It has been studied that the membrane permeability is closely related to microbial particle size and soluble foulants like EPS in the mixed liquor significantly affect to membrane fouling (Kim et al., 2001; Lim et al., 2003; Lee et al., 2007). Therefore, the effects of coagulants on sludge properties such as floc size, zeta potential and permeability characteristics such as membrane resistance and permeate flux were investigated to elucidate their relations.

4.3.1.1 Particle size distribution

Batch experiments were conducted to determine the optimum dosage of coagulants, in which the change of particle size based on the volume equivalent diameter in mixed liquor of MBR process was investigated in terms of various dosages of two coagulants (Figure 4.4). Regarding the effect of PAC injection, measured median particle size ranged from 110 nm to 488 nm and no significant difference between dosages of 0 mg/L (control) and 5 mg/L was observed. However, as the dosage of 10 mg/L was injected particle size was 2 times larger than control, and the highest result was found in dosage of 20 mg/L. Also, it was apparent from our study that floc size in mixed liquor decreased with 50 mg/L of dosage, indicating injection of PAC over the optimum dose was unnecessary. This could be attributed to the conversion of charge on the surface of the flocs from near neutral towards positive caused by excessive addition of electrolytes (Pinotti et al., 2001). Particle size distributions by chitosan showed 110, 158, 322, 440 and 375 nm in 0, 1, 2, 5, 10 and 20 mg/L, respectively. Although the similar tendency shown in PAC experiment by overdose was obtained in 20 mg/L of chitosan, the largest particle size of chitosan injection (10 mg/L) was slightly lower than that of PAC. Similar results were found by Ji et al. (2010) that organic polymeric flocculants like chitosan showed stronger effects on biomass morphological properties and at Al^{3+} salts dosages beyond certain levels, a decrease in mean floc size occurred. These results can be explained by the fact that both coagulants having a positive charge combine to the negative charged surface of MBR sludge and thus aggregation of neutralized sludge flocs can be occurred in the mixed liquor to make them larger. Also, Lee et al. (2007) demonstrated that the neutralized sludge flocs may attract each other by a charge neutralization mechanism to produce larger flocs.

Generally, in combination of MBR and coagulation process, improved permeability is achieved by increase of sludge flocs larger than membrane pore size that is induced by injection of coagulation, which can reduce the effect of irreversible fouling such as pore blocking and sever cake layer. According to several authors, the addition of a coagulation agent generates greater binding forces between the SMP and the bacteria, producing a larger mean particle size of MBR sludge (Wu et al., 2006; Nguyen et al., 2012). Therefore, injection of coagulants at optimum dosage is effective to reduce membrane fouling in MBR process due to enlargement of small colloidal particles, which are known to be as a major contributor to membrane fouling, thereby improving the permeability performance (Fan et al., 2007).



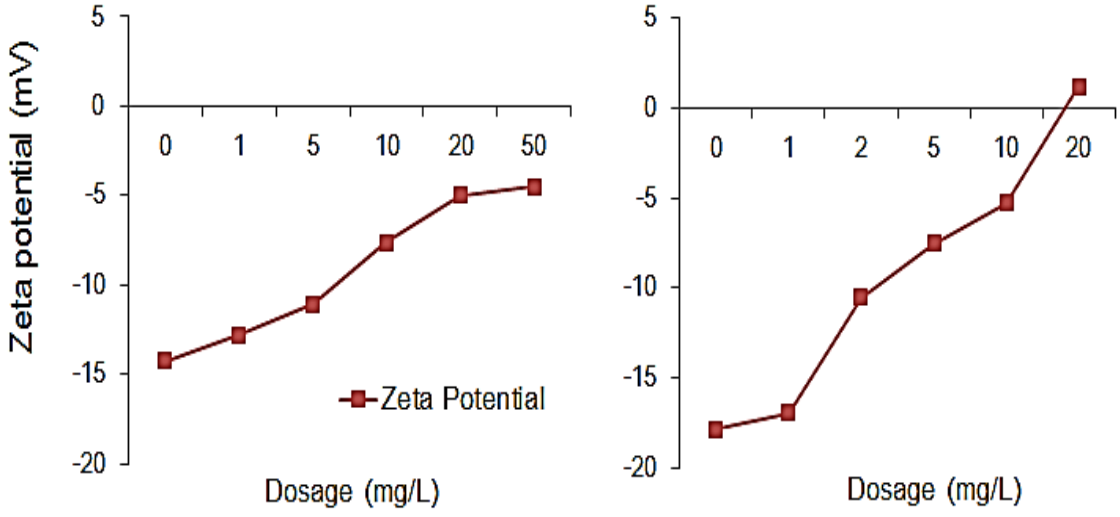
(a) PAC (b) Chitosan

Figure 4.4 The change of particle size distribution

4.3.1.2 Zeta potential

The effect of coagulants on physical properties of MBR sludge was investigated by measuring surface charge of sludge flocs in the mixed liquor. Figure 4.5 shows the change of zeta potential in terms of different dose of two coagulants. Zeta potential by PAC injection increased from -14.7 to 4.1 mV as PAC dosage increased from 0 (control) to 50 mg/L. Similar tendency was observed in another experiment on chitosan injection, whereas positive charge on the surface of sludge flocs was found in dosage with 20 mg/L of chitosan. Nearly neutral and positive charge was obtained in PAC of 50 mg/L and chitosan of 20 mg/L, respectively. It can be described that these coagulants having

cationic characteristic decrease negative charge by sludge flocs and change properties of surface charge at the optimum dosage. It is interesting to note that the surface charge of sludge flocs changed to positive charge with increasing chitosan dosages, which is consistent with the results of particle size distributions because particles with zeta potential of near neutral or mildly charged surfaces tend to be aggregated. Ji et al. (2010) also reported that due to the adoption of cationic flocculants, positive charges generated from flocculants hydrolysis neutralized the negative charges on the surface of the biomass flocs. At the minimum surface charge, in which zeta potential is around zero, the effective coagulation was achieved by charge neutral, thus can result in enhanced performance of membrane permeability.



(a) PAC (b) Chitosan

Figure 4.5 The change of zeta potential

4.3.2 Variations of permeability properties by coagulation

From the result of the variations of sludge properties by coagulation, 20 mg/L of PAC and 10 mg/L of chitosan were found to be appropriate dosage considering both particle size and surface charge and thus the optimum dosages of coagulants were adopted to investigate permeability performance and fouling resistance for applicability of long-term operation in coagulation-MBR process.

4.3.2.1 Permeability performance

The permeability performance of selected dosage was investigated at constant operating flux of 10.4 L/m^2·h in continuous operation for 2 months. Figure 4.6 illustrates the normalized permeability, in which permeate flux was divided by operation pressure to better understand the relations between two parameters. As can be seen in Figure 4.6, the injection of PAC and chitosan showed significant impact on the permeability performance. The normalized permeability was 2.3 and 2.8 times larger in PAC and chitosan than that in the control. For the control, the time required to reach the critical flux was 34 d and thus, backwashing was inevitable after that time, whereas backwashing was not needed in the operation of PAC and chitosan. In particular, at the time required to reach the critical flux, the TMP of PAC and chitosan were 13.7 and 11.1 kPa and 2-3 times lower TMP than the control was observed. These results were consistent with recently conducted studies. Zhang et al. (2015) suggested the effect of ferric and ferrous iron addition for fouling reduction. For example, operation of the control was maintained for 40 d, while significantly increased time was observed in the addition of coagulants. The sustainable filtration time at the optimum dosage was nearly 6.7 times higher than control experiment in terms of most studied additives such as aluminum or iron based coagulants (Ji et al., 2010). The result on permeability performance means that a longer period of operation can be maintained by application of both coagulants to MBR process.

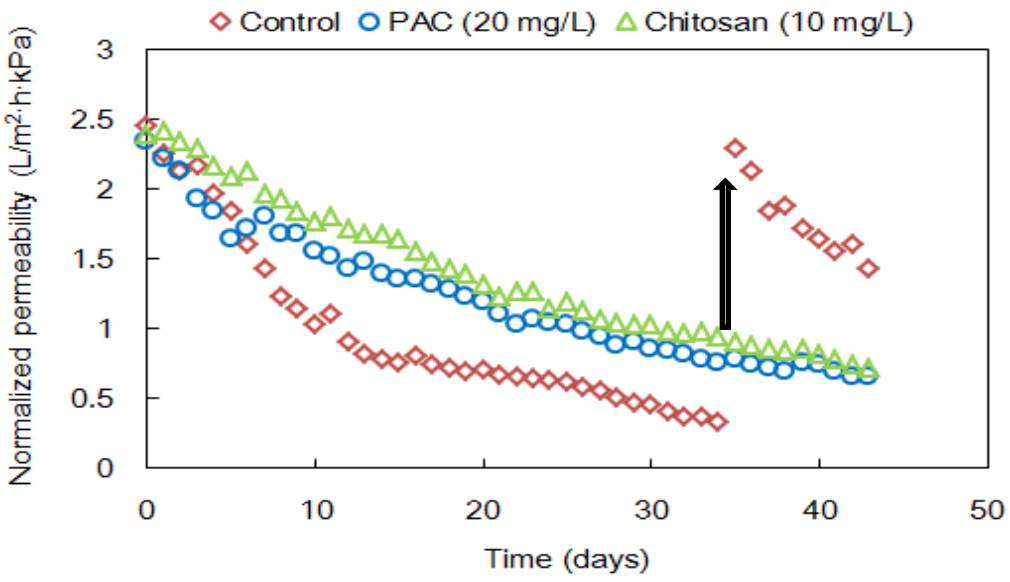


Figure 4.6 Normalized permeability by coagulation

Arrow represents backwashing time with tap water when the TMP reached to critical flux

4.3.2.2 Permeability resistance

Permeability resistance of control, PAC and chitosan was estimated to assess fouling characteristics and each component (i.e., intrinsic membrane resistance, cake resistance and irreversible resistance) affecting membrane filtration, which are represented in Table 4.2. Because critical flux was reached at 34 d without injection of coagulants, specific resistance of each case at that time was investigated. Compared with injection of PAC and chitosan, total resistance was higher in control, which indicates that as the coagulants were injected into the mixed liquor R_t in Eq.4.2 decreased due to the remarkable attenuation of the sum of R_c and R_f. As PAC added, fraction of R_c had 54% and which was 10% higher than control, while fraction of R_f was 11% lower than control. It was consistent with the experiment of chitosan, in which fraction of R_c was the highest among all studied resistance value (59%).

Since this experiment was conducted using the same influent sources or operating conditions and even equivalent MLSS concentration except for addition of coagulants, it can be described that the effect of irreversible fouling decreased in continuous operation by injection of coagulants. Although fouling caused by cake layer increased in both operations, permeability performance can be periodically recovered by rinse with tap water, which was significantly related with pervious results on normalized permeability and the time required for reaching the critical flux.

Table 4.2 Permeability specific resistance by coagulation

Coagulants	Permeability resistance (10^{-11} x m^{-1})			
	R_t	R_m	R_c	R_f
Control	30.4	3.2 (11%)	13.5 (44%)	13.7 (45%)
PAC	20.5	2.4 (12%)	11.1 (54%)	7 (34%)
Chitosan	17.2	1.7 (10%)	10.2 (59%)	5.3 (31%)

Fraction of specific resistance are represented in brackets

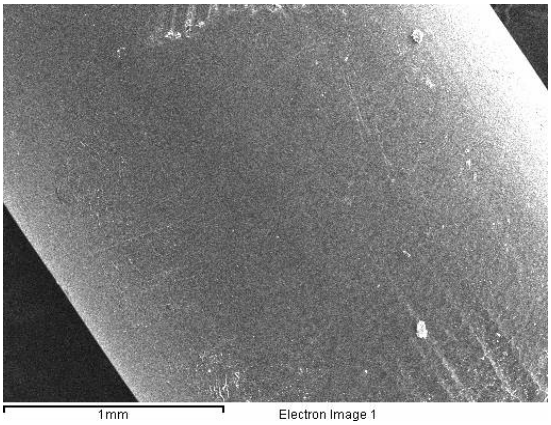
4.3.2.3 SEM and EDX

Fouling characteristics of membrane surface was analyzed according to the SEM images and Figure 4.7 shows that surface of new membrane (a), fouled membrane without addition of coagulants (b), fouled membrane of PAC (c) and chitosan (d), respectively. As can be seen in Figure 4.7 (b), cake layer built up on the membrane surface seemed to be dense, which can be caused by bacterial clusters covered with foulants such as bound and soluble EPS. Also, the elemental analysis was carried out to identify chemical elemental compositions in the fouling layer of membrane using EDX analytical technique and the results are shown in Table 4.3. The main elements of membrane covered with cake layer were fluorine (F) due to the effect of membrane materials, except for oxygen (O) and carbon (C) that are either the major components of the organic phase or typical characteristic used in formulating organic membrane. It is interesting to note that as chitosan was injected, relatively small amount of inorganic elements were detected in comparison to the control.

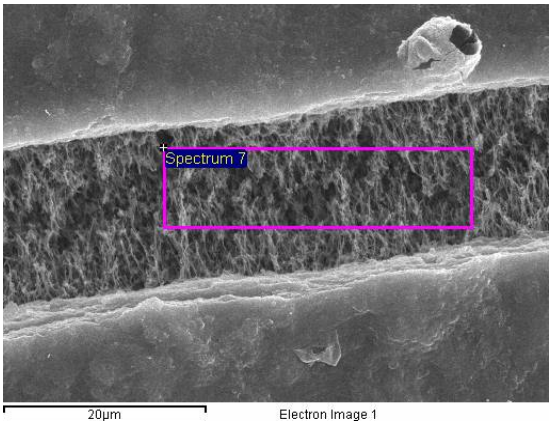
It was shown that even though component of Al increased with injection of PAC due to the floc formation between aluminium ions of PAC and negative charged sludge, other inorganic elements decreased, which was the similar result with injection of chitosan. It has been reported that the existence of these inorganic materials had a significant effect on formation of cake layer. For example, SEM-EDX analysis indicated that Si, Ca, Mg, Al and Fe were the origin of inorganic fouling, which might affect structure of cake layer (Meng et al., 2007).

4.3.2.4 EPS and SMP

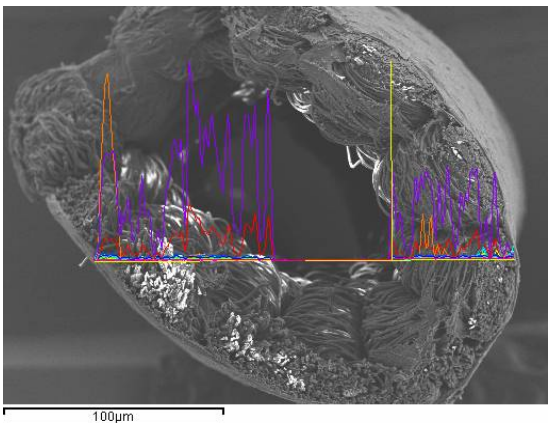
Table 4.4 shows the results on analysis of EPS and SMP. The concentrations of EPS in injection of PAC, chitosan and control showed 65.4, 55.2 and 45.3 mg/g_{vss}, respectively, suggesting that compared with control, the EPS concentrations increased by addition of both coagulants. SMP concentration of 21.5 mg/L in control appeared to be the highest, while as PAC and chitosan added the SMP concentration decreased to 13.3 and 19.2 mg/L. Variation of concentrations between EPS and SMP in terms of injection of coagulants showed conflicting results, which indicates soluble foulants present in the mixed liquor could be trapped by coagulants and thus the decreased SMP concentration was achieved when both coagulants were injected, but the lower concentration was proven in PAC having more positive charges than chitosan.



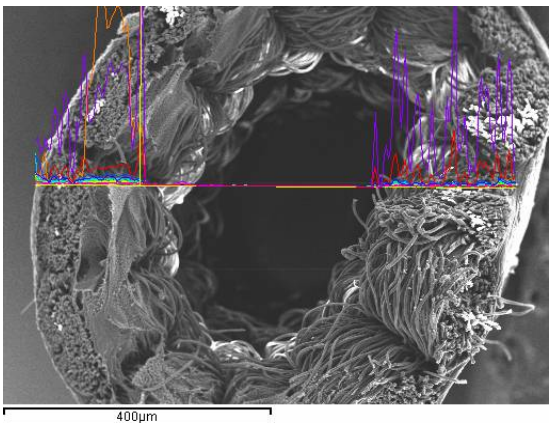
(a) New membrane



(b) Fouled membrane (control)



(c) Fouled membrane (PAC)



(d) Fouled membrane (chitosan)

Figure 4.7 The images of SEM analysis

Table 4.3 EDX analysis of fouled membrane

Elements	New	Control	PAC	Chitosan
	Unit (%)			
C	17.18	17.08	17.51	17.06
O	45.02	44.00	44.55	44.57
F	37.80	34.03	33.21	35.41
Si	ND	1.32	0.85	0.91
Mg	ND	1.11	0.80	0.40
P	ND	0.78	0.61	0.64
Al	ND	0.83	1.86	0.42
Ca	ND	0.32	0.20	0.13
Mn	ND	0.49	0.41	0.38
Na	ND	0.04	ND	0.08

Table 4.4 Results of EPS and SMP concentration

Coagulants	EPS	SMP
	(mg/g_{vss})	(mg/L)
Control	45.3	21.5
PAC	65.4	13.3
Chitosan	55.2	19.2

It can be also described by increased EPS concentration and the lower fouling rate can be attributed to the attenuation of SMP concentration and results of our previous study on permeability resistance and the effect of inorganic components in cake layer on membrane surface.

4.3.3 Removal of PPCPs by batch experiment

We conducted this study to elucidate the properties of coagulation affecting fouling characteristics and filtration performance. The optimum dosages for each coagulant were determined previously. However, application of coagulation in the removal of PPCPs still remains as a debatable issue and thus evaluation on removal of PPCPs was performed by batch experiments.

4.3.3.1 Effect of coagulant types and dosages

The effect of different dosage for each coagulant was studied and the compounds which were strongly influenced by coagulation are shown in Figure 4.8. The removal efficiencies ranged from -5% for furosemide to 9% for sulfamethoxazole at 1 mg/L of PAC, but as can be seen in Figure 4.8, higher removal performance was observed with increasing dosages of PAC, which means that some compounds were removed due to aggregation by coagulation between the compounds that are mainly present in liquid phase and the mixed liquor. Diclofenac had the highest removal among target compounds and removal efficiency increased by 92%, whereas sulfamethoxazole, ketoprofen and mefenamic acid showed higher removal efficiencies when 10 mg/L of PAC used, and no significant efficacy was observed beyond the dosage over 10 mg/L. The removal of furosemide was found to be effective in 20 mg/L of PAC, while it decreased by 55% in 50 mg/L of PAC. It indicates that adsorption of these compounds

by PAC reached the equilibrium condition and when optimum dosage was used their removal showed the highest performance. For instance, diclofenac having the persistence toward MBR treatment and variable removal were well eliminated by coagulation (Hai et al., 2011; Tadkaew et al., 2011), which was in good agreement with our results. On the other hand, removal efficiency was independent of the injection of chitosan. Any improvement of removal performance was not shown in not only the compounds which were efficiently removed by PAC, but also other compounds. Even though we could identify the characteristics of chitosan affecting MBR sludge from the study on increased particle size and attenuation of soluble foulants caused by trapping, removal of PPCPs was not related with adsorption properties of chitosan.

In short, we verified that for removal of PPCPs, PAC was superior to that of chitosan, and the highest removal performance was achieved in dosage of PAC 20 mg/L.

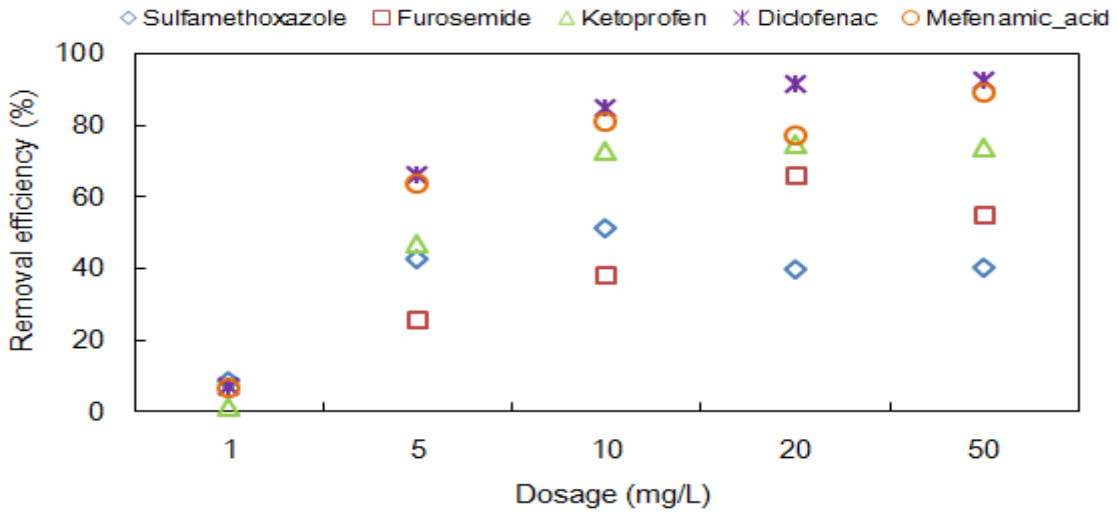


Figure 4.8 Removal efficiency by PAC

4.3.3.2 Effect of pH changes and sludge characteristics

Some compounds which were eliminated by PAC had common physicochemical properties (i.e., ionisable characteristics). Since these ionisable compounds were strongly dependent on the change of pH, it is expected that if there is any variations of adsorption tendency as a function of pH change, enhanced removal performance of PPCPs will be achieved. Therefore, relations of adsorption tendency that was represented as log k_d value and change of pH in batch experiment of PAC were studied and the effect of coagulation on sludge characteristics (MBR versus CAS sludge) was

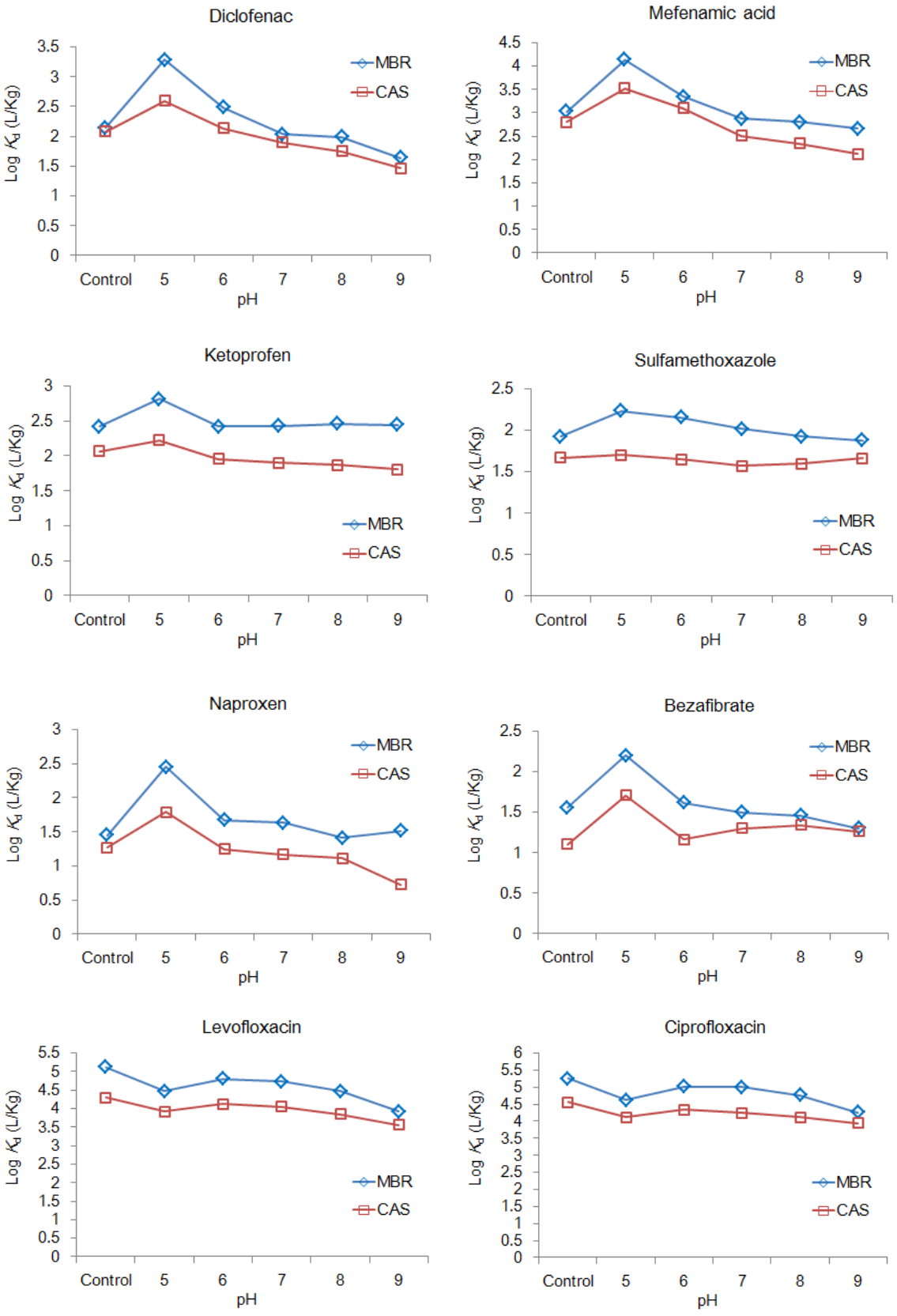


Figure 4.9 Log K_d value by pH change in MBR and CAS sludge

investigated. Batch experiments were conducted by adjusting pH value ranged from 5 to 9 or control (no pH control) with 0.1M HCl and NaOH solution. 20 mg/L of PAC was injected into Jar-test devices of 2L and MLSS concentrations of MBR and CAS were 7,500 mg/L and 2,500 mg/L, respectively. Figure 4.9 shows the log K_d value by pH change in MBR and CAS sludge. Log K_d value of furosemide was not calculated due to low LOQ of solid sample, while four ionisable compounds such as diclofenac, mefenamic acid, ketoprofen and sulfamethoxazole showed the highest log K_d value at pH 5, particularly, diclofenac and mefenamic acid had higher log K_d values with 3.3 and 4.1 at the pH 5. These values decreased from pH 6 and the lowest values were found at the pH 9. These values could be attributed to their physicochemical properties under low pH conditions rather than intrinsic hydrophobicity. As can be seen in Table 2.1, these compounds are characterized by low p*K*a value, ranging from 4.2 to 5.8, so that they can exist predominantly as neutral species at pH 5, allowing them to adsorb to the activated sludge (Tadkaew et al., 2010). In a similar study, Carballa et al. (2003) summarized that 50-70% of diclofenac was found to be eliminated by coagulation and flocculation system using ferric chloride and aluminium sulphate. Although the similar trend was obtained in ketoprofen and sulfamethoxazole, compared with former two compounds, the variations of log K_d values were not considerably changed. With regard to naproxen and bezafibrate, their log K_d values were not much higher than other ionisable compounds, but they also showed high adsorption affinity at pH 5. On the other hand, log k_d values of fluoroquinolone antibacterials such as levofloxacin and ciprofloxacin that have reported significant adsorption tendency with biomass developed in biological treatment process decreased with increasing pH, in which adsorption tendency was found to be the highest in control, indicating that it was not dependent on the change of pH in non-ionisable compounds or compounds having high adsorption affinity caused by a relatively high hydrophobicity.

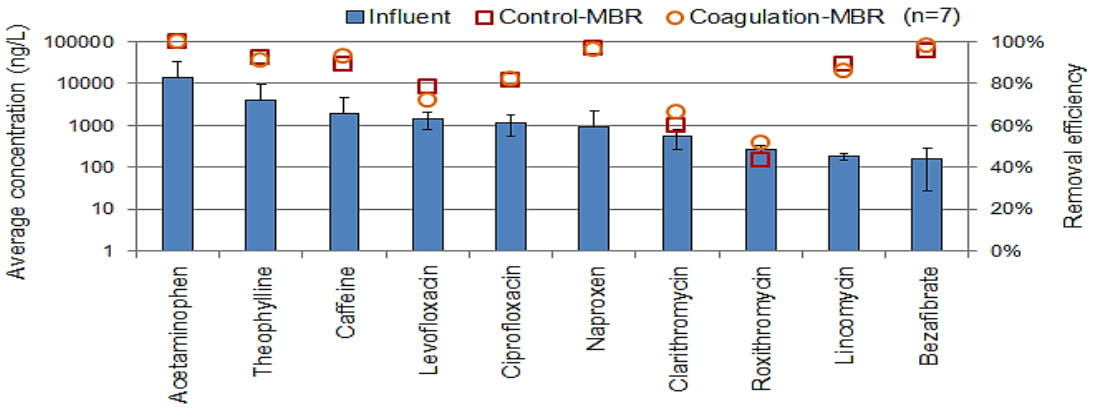
Furthermore, compared with CAS sludge, adsorption tendency of target compounds that was adjusted by pH control was higher in MBR, which can be explained by the reason that MBR process had higher adsorption affinity than CAS sludge due to increased specific surface area by smaller particle size which was developed in MBR operation. Also, microbial diversity could be achieved in MBR because 3 times higher MLSS concentration was used and thus, coagulants can be greatly adsorbed on the MBR sludge. However, it is very important to note that our study was carried out in the condition of pH 6.8 (±0.3), in which ionisable compounds were independent of variations of pH, suggesting that the removal of these ionisable compounds by coagulation might not be effective under typical MBR conditions.

4.3.4 Removal of PPCPs by loge-term operation

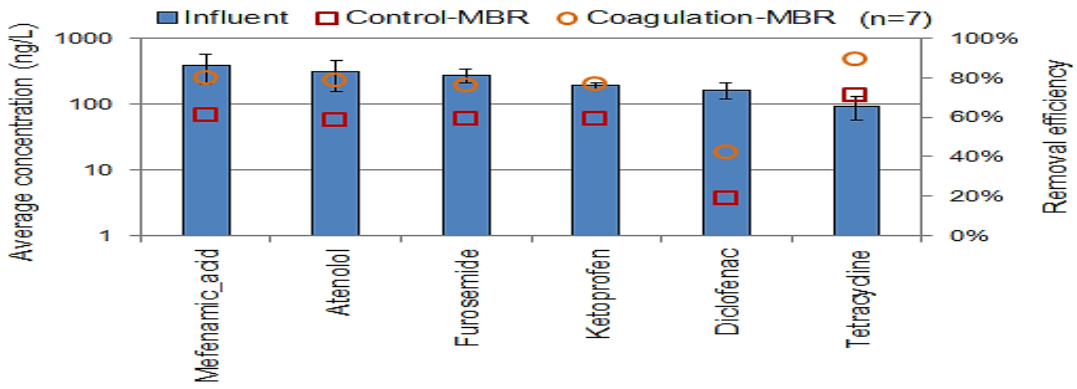
20 mg /L of PAC was determined as the optimum dosage from various experiments of Chapter IV, and therefore, the study on removal efficiencies and characteristics between coagulation-MBR and control-MBR was performed by directly comparing two systems and identifying the improvement of biodegradability using the mass balance of each process.

4.3.4.1 Comparison of coagulation-MBR and control-MBR

Figure 4.9 shows the removal efficiencies of target compounds by long-term operation, in which evaluation on coagulation-MBR can be divided into two groups based on the degree of removal: firstly, the compounds having similar removal efficiencies between two processes and secondly, the compounds, in which better removal by coagulation-MBR is achieved.



(a) The compounds with comparable removal efficiencies



(b) The compounds with higher removal in coagulation-MBR

Figure 4.10 Removal efficiency of PPCPs by long-term operation

As can be shown in Figure 4.10 (a), removal of PPCPs such as acetaminophen, theophylline, caffeine, naproxen and bezafibrate appeared to be significantly efficient in both processes, with average removal performance over 90%. Also, macrolide antibiotics (clarithromycin and roxithromycin) and fluoroquinolone antibacterials (ciprofloxacin and levofloxacin) showed moderate removal in both processes, in which no significant difference on removal efficiencies between coagulation-MBR and control-MBR was observed, which indicates that although coagulation is considerably related with adsorption tendency, coagulation did not influence on the removal performance of the compounds with high adsorption affinity like ciprofloxacin and levofloxacin. The compounds that showed higher removal efficiency in the batch experiments by coagulation, such as mefenamic acid, furosemide, ketoprofen and diclofenac, indicated removal efficiencies of 61%, 59%, 59% and 19% in control-MBR. Compared with control-MBR, removal of these compounds increased to 80%, 76%, 77% and 42%.

It is noteworthy to mention that in comparison with control-MBR, removal performance of coagulation-MBR increased from 58% to 78% for atenolol, and from 71% to 89% for tetracycline. These compounds showed enhanced removal performance by coagulation, but they were not removed in previous batch test, suggesting that tetracycline which showed high adsorption tendency can be efficiently removed in long-term operation, while removal of atenolol which was mainly removed by biodegradation in previous study can be attributed to the effect of other mechanisms like biodegradation, in addition to adsorption which seems to be a primary removal pathway in coagulation. From the results of coagulation-MBR and control-MBR, enhanced removal performance in some compounds was identified; they included not only ionisable compounds which were significantly attenuated in batch experiment, but also the compounds having low log K_{ow} and high adsorption tendency, and therefore, these results may have been due to the enhanced biodegradability that was arisen from coagulation as well as the effect on adsorption by hydrophobicity and physicochemical properties.

4.3.4.2 Improvement on biological activity by coagulation

The benefits of MBR include better control of biological activity, but compared with CAS system, oxygen uptake rate (OUR), which is represented as the volumetric oxygen consumption rate, is lower in MBR process because it can considerably related with F/M ratio, which is generally 3-6 times higher in CAS process due to low MLSS

concentration. If bioactivity of MBR process increases as coagulation is added, it will be beneficial in improving the performance of biodegradation and thus the effect on microbial activity and oxygen transfer by PAC and chitosan was investigated by measuring uptake rate by microorganisms. OUR profile for each experiment is illustrated in Figure 4.11 and the summary of specific oxygen uptake rate (SOUR) and specific nitrification rate (SNR) are listed in Table 4.5. Because oxygen is required for microorganisms to decompose organic compounds in a biological treatment process, biological activity can be characterized by SOUR (Han et al., 2005).

In comparison with control, average OUR in PAC and chitosan showed high performance, rates with 1.21 or 1.28 times in respectively, these results are consistent with previous reviews. For example, Guo et al. (2010) reported that regarding OUR and SOUR, all studied different additives like PAC, chitosan and $FeCl_3$ showed significant improvements, as well as slightly increased DOC performance. OUR and filtration time have reached 1.5 times and 2.5 times higher than control test, respectively (Nouri et al., 2014). Also, the variations of microbial activity according to addition of coagulation were found in SNR, for which slightly increased rate was obtained in both coagulants.

It can be explained by the fact that the membrane of MBR process can provide physical barriers for retention of organic compounds adsorbed on PAC, as well as solids and bacteria in the mixed liquor, which make it possible for microorganisms to growth on the surface of membrane, leading to achieve the high biological activity. These phenomena cannot be described in the absence of either the effect of membrane or adsorbent.

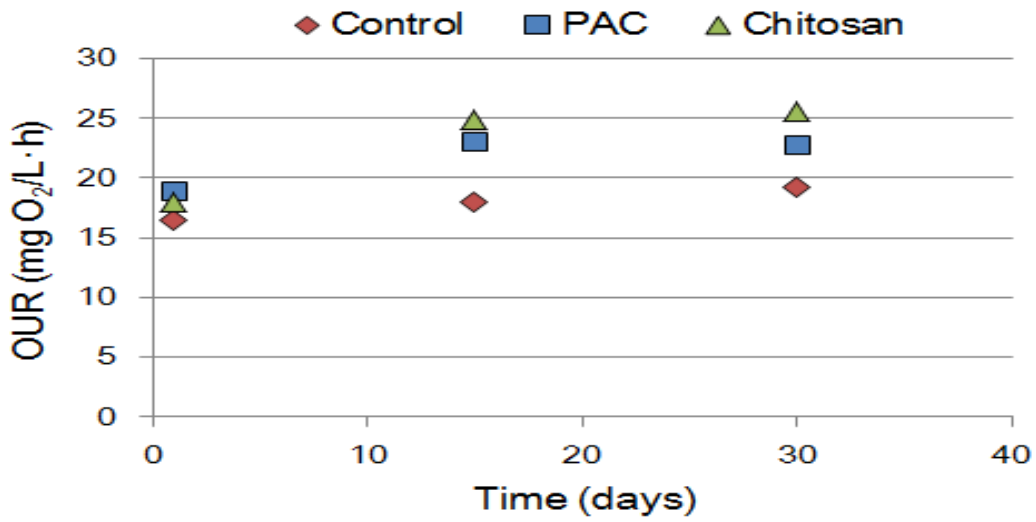


Figure 4.11 OUR profile of control, PAC and chitosan

Table 4.5 The values of OUR, SOUR and SNR

Specification	Average OUR	Average SOUR	SNR
	mg O_2/L· h	mg O_2/g_{MLVSS}·h	mg NO_3-N/g_{MLSS}·h
Control	17.90 (±1.33)	3.09 (±0.23)	1.42
PAC	21.59 (±2.35)	3.72 (±0.41)	1.59
Chitosan	22.80 (±4.19)	3.93 (±0.72)	1.48

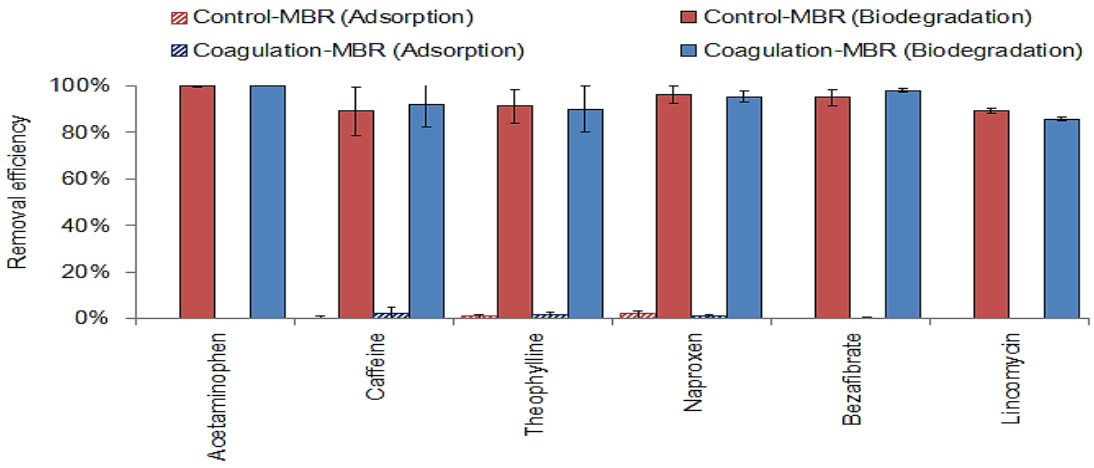
4.3.4.3 Evaluation on biodegradability enhancement

In order to better clarify relations between enhanced microbial activity and removal of PPCPs, mass balance was evaluated by comparing two main removal pathways. These results are shown in Figure 4.12 using three distinguished categories. As can be seen in Figure 4.12 (a), the compounds which have been reported that they are readily biodegradable in MBR process showed removal efficiencies ranged from 99.9% for acetaminophen to 85.7% for lincomycin. Since these compounds were equally well removed in both systems, it can be difficult to discuss the effect of coagulation in terms of removal of PPCPs.

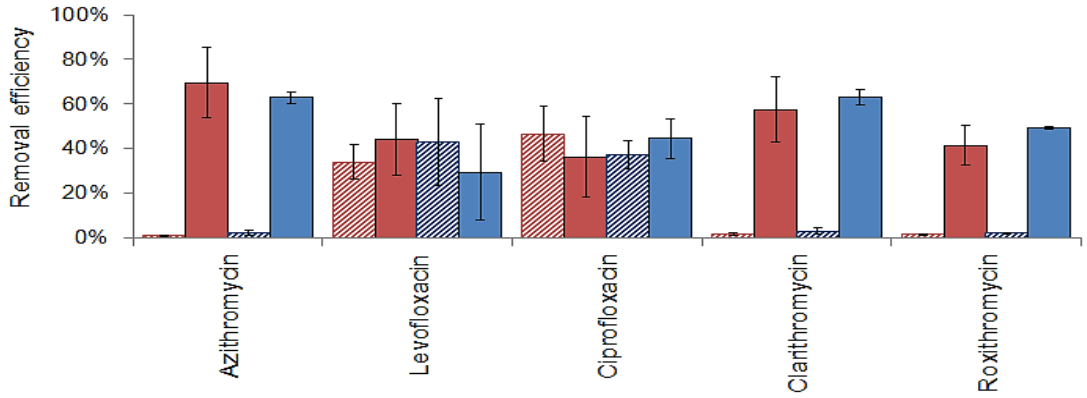
The similar removal performance was obtained in macrolide and fluoroquinolone compounds, with the maximum removal of 88.1% for ciprofloxacin and the minimum removal of 43.6% for roxithromycin, although the removal efficiencies in most cases were far from complete. Particularly, among these compounds (Figure 4.12 (b)) removal of adsorption was superior for levofloxacin and ciprofloxacin that were characterized by high adsorption tendency, whereas for azithromycin, clarithromycin and roxithromycin their removal was not significant for adsorption, with removal efficiencies less than 3% in both cases, which was very similar to those of previous studies. However, no consistent differences were seen in removal of biodegradation and even adsorption, showing that the removal efficiency of these compounds does not seem to be improved appreciably by coagulation.

Figure 4.12 (c) shows the compounds which showed greater removal in coagulation-MBR. Removals of biodegradation in control-MBR were 58.1, 55.1, 56.8, 25.2, 55.5, 55.1, and 15.5% for ketoprofen, sulfamethoxazole, mefenamic acid, tetracycline, atenolol, furosemide and diclofenac, respectively, which increased up to 76.3, 64.8, 76.1, 45.8, 78.0, 74.9 and 38.1% for these compounds in coagulation-MBR. With the exception of tetracycline, enhanced biodegradation was found in most

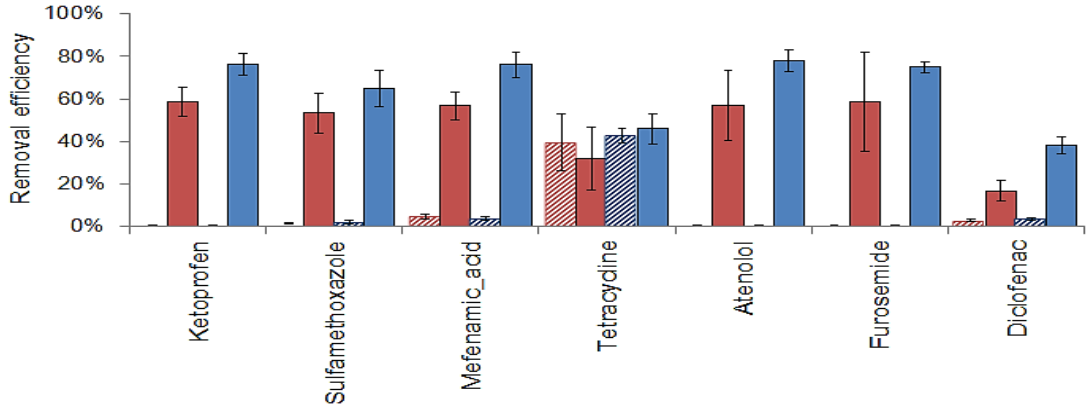
compounds of Figure 4.12 (c), whereas removal of tetracycline was caused by both increased adsorption and biodegradation.



(a) Readily biodegradable compounds



(b) Macrolide and fluoroquinolone compounds



(c) Well removed compounds by coagulation-MBR

Figure 4.12 Comparison on removal performance of coagulation-MBR and control-MBR

Sample analysis (n=7) and error bars are represented by standard deviation of the individual data.

Enhanced bioactivity that was influenced by microbial growth on the membrane surface as PAC was added to MBR Process was observed, in which microorganisms may be forced to biodegrade or metabolize the poorly degraded compounds which are not expected to remove in the absence of coagulation. This is one explanation why removal of some compounds can be superior in coagulation-MBR and why they can be achieved with improvement of biodegradation. It also can be evidenced by our previous findings on the reduction of fouling rate and decreased SMP concentration.

Since there does not seem to have been any research to focus either the removal fate and performance of pharmaceuticals or investigation on their removal characteristics by application of coagulation, comparison of other studies was impossible to evaluate whether increased removal efficiency in coagulation-MBR is contributed to enhanced biodegradability. However, our results could show the improved biodegradability in terms of removal of PPCPs during long-term operation and identify the potential to combination of coagulation and MBR process which may be more effective in eliminating PPCPs.

4.4 Conclusions

The effect of coagulation in MBR process was evaluated in terms of the variations of sludge properties and permeability performance through membrane resistance and fouling characteristics. Moreover, the comparative study using two processes based on the removal characteristics and performance of PPCPs was conducted to understand removal mechanisms and evaluate the applicability of coagulation-MBR for long-term operation. The main conclusions can be drawn as follows:

1) Addition of coagulants had significant impact on sludge properties. In terms of the variations of these characteristics, 20 mg/L of PAC and 10 mg/L of chitosan were selected as the optimum dosage, in which larger particle size and increased zeta potential were identified.

2) Permeability performance increased in accordance with addition of coagulants and membrane fouling was significantly reduced due to the attenuated irreversible fouling by decrease of SMP concentration and inorganic materials of cake layer or membrane surface.

3) From the results of batch experiments, PAC was superior to chitosan in the removal of PPCPs, in which some compounds having ionisable properties were greatly eliminated. Also, higher adsorption tendency was observed in MBR sludge in comparison to CAS sludge and it was found to be the highest k_d value at pH 5. However, no significant difference was obtained at pH 7, indicating that adsorption tendency was not improved under typical MBR condition of around pH 6.8.

4) Compared with control-MBR, removal of some compounds was found to be effective in coagulation-MBR. It can be proven by the results on comparison of mass balance between two systems, suggesting that increased removal efficiencies could be mostly attributed to the enhanced biodegradability.

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Chapter Ⅴ

Classification of PPCPs by Removal Pathways

5.1 Introduction

The vast majority of literatures published in the field of PPCPs removal have pointed out the fate of PPCPs in WWTPs, in which samples of the different WWTPs units like influent, effluent and sludge of bioreactors were investigated to determine overall removal efficiency of compounds as well as additional treatment processes such as disinfection and sterilization, without emphasizing on the understanding of the removal pathways. During the last decade, however, many authors have focused on not only occurrence and removal performance of PPCPs, but also their mechanisms in WWTPs to clarify removal characteristics. In some works, the importance of adsorption and volatilization in removal of PPCPs was significantly considered (Clara et al., 2005; Kupper et al., 2006; Joss et al., 2006; Yu et al., 2013). According to Li et al. (2010), biodegradation and adsorption were the major removal routes for the target antibiotics, while volatilization and hydrolysis were negligible. Also, adsorption onto sludge as the main removal mechanisms were examined in lab-scale batch experiments, in which adsorption was found to be less than 3% and negligible (Wick et al., 2009). Abegglen et al. (2009) suggested the fate of PPCPs in a single-house MBR. It was highlighted that biological transformation was the main removal process while adsorption to the activated sludge was minor mechanism for most substances due to the low sludge production at high SRT.

As shown above, many authors have reported the reaction constants of various PPCPs with different reaction equations. However, they are still limited and cannot be described merely as common kinetic models due to each different characteristic of target compounds. Although, moreover, MBR process have been widely used for efficient removal of PPCPs, which allows better removal performance than CAS system,

particularly for biodegrading the persistent compounds (Kimura et al., 2005; Radjenovic et al., 2009; Sipma et al., 2010), it is still not clear why MBR process is more effective in the biodegradation and adsorption than CAS.

Therefore, in Chapter V, batch experiments were carried out to elucidate the removal pathways in MBR process by determining the biodegradation kinetic constant and adsorption constant of selected compounds and then they were classified into each group according to three different reactions: 1) biodegradation, 2) adsorption and 3) simultaneous removal which includes biodegradation in both liquid and solid phase. Also, they were compared to identify the differences between the biomass developed in MBR and CAS system.

5.2 Materials and methods

5.2.1 Experimental design

Batch experiments were performed to evaluate removal routes using four reactors with different conditions, as described in Table 5.1. Four 500 mL flasks with 400 mL MBR sludge were simultaneously run at 25 ℃ with pH ranged from 6.7 to 7.5 and constantly agitated on a shaking plate at 100 rpm. MBR sludge from pilot-scale MBR plant which is located in K city of Japan, operating at SRT of 23 (±5) d and MLSS concentration of 12,000 (± 200) mg/L was used for each study. In the case of R2, R3 and R4, sodium azide (NaN_3) was used to inactivate bioactivity of microorganisms, whereas it was not added in R1 to differentiate between biodegradation and adsorption. In general, since an inhibition of bioactivity is known to be obtained by addition of the appropriate quantity of NaN_3 (Xu et al., 2008), concentrations of 0.1, 0.5, 1 and 2% (NaN_3, w/v) was evaluated as preliminary study by measuring COD_{cr} and ammonia nitrogen (NH_3-N) concentration. With the exception of R4, dissolved oxygen concentrations higher than 4 mg/L were constantly supplied to maintain aerobic conditions from aeration pump. All reactors were covered with aluminium foils to avoid possible photolysis and standard solution was spiked as final concentration of 100 μg/L. Also, samples of 20 mg/L were collected after 0, 1, 2, 5, 10, 24, 48, 72 and 96 h to quantify concentrations of PPCPs in both liquid and solid phase. The concentrations of target compounds were determined using the pretreatment and analytical methods as described in 3.2.2. From the results of batch experiments, removal pathways can be

calculated based on the mass balance of each reactor as follows:

Biodegradation = R1 - R2

Adsorption = R2 - R3

Volatilization = R3 - R4

Hydrolysis = R4

Table 5.1 Batch experimental design

Reactor #	Activated sludge	NaN_3	Standard spike	Aeration	Removal routes[a]
R1	+[b]	-	+	+	B+A+V+H
R2	+	+	+	+	A+V+H
R3	-	+	+	+	V+H
R4	-	+	+	-	H

[a] B-biodegradation, A-adsorption, V-volatilization and H-hydrolysis.

[b] + showed with or added, - showed without or not added.

5.2.2 Description of reaction equations

5.2.2.1 Biodegradation kinetic models

Biodegradation can be represented by three biodegradation kinetic models such as zero-order (Eq.5.1), first-order (Eq.2.2) and second-order (Eq.5.2) kinetics (Schwarzenbach et al., 2003; Urase et al., 2005; Joss et al., 2006; Li et al., 2010; Costa et al., 2012). Therefore, in this study, these kinetic models were evaluated in terms of the goodness of fit with observed data to better explain reactions caused by biodegradation.

$$\frac{\mathrm{dC}}{\mathrm{d}t} = -k_0 \leftrightarrow \mathrm{C}_t = \mathrm{C}_0 - k_0 \cdot t \qquad \text{(Eq.5.1)}$$

$$\frac{\mathrm{dC}}{\mathrm{d}t} = -k_2 \cdot \mathrm{C}^2 \leftrightarrow \mathrm{C}_t = \mathrm{C}_0/(1 + C_0 \cdot k_2 \cdot t) \qquad \text{(Eq.5.2)}$$

Where, C_0 is initial concentration of PPCPs (ng/L); C_t is concentration of PPCPs at time t (ng/L); k_0 is the zero-order rate constant (ng/L·h); and k_2 is the second-order rate constant (L/ng·h), respectively. Also, half-lives, a reaction describes the time needed for half of the reactant to be depleted, are given by $C_0/2 \cdot k_0$ (h) and $1/k_2 \cdot C_0$ (h).

On the other hand, PPCPs may be not only directly biodegraded from liquid phase, but also degraded from solid phase after adsorption onto sludge and thus, target compounds can be simultaneously removed via degradation from two-phase (both solid and liquid phase). Accordingly, this concept can be properly described by the variations of total concentrations (dissolved and particulate) in batch experiments using Eq.5.3 (henceforth simultaneous removal) (Mazioti et al., 2015). Also, pseudo first-order biodegradation constant, k_{bio} ($L \cdot g_{MLSS}^{-1} \cdot d^{-1}$), normalized to biomass concentration can be determined based on the pseudo first-order kinetics (Ziels et al., 2014).

$$\ln \frac{C_t}{C_0} = -k_{bio} \left(\frac{MLSS}{1 + K_d MLSS} \right) \cdot t \qquad \text{(Eq.5.3)}$$

Where, K_d is sludge-water distribution coefficient (L/kg); C_0 is initial total PPCPs concentration including liquid and solid phase (ng/L); C_t is total PPCPs concentration at time t (ng/L); and MLSS is MLSS concentration of bioreactor (g/L).

5.2.2.2 Adsorption kinetic models

Adsorption is assumed as the result of two transport processes with opposite directions. As represented in Eq.2.1, adsorption coefficient is defined as the ratio between the concentration of the adsorbate and the adsorbent, in which the sludge-water distribution can be determined. Moreover, even though adsorption rate can be limited by diffusion in the fluid or inside in the solid phase or by a combination of two limitations, the velocity of adsorption can be represented by the following model, herein the transfer of solute from the water to the boundary layer of fluid immediately adjacent to the external surface of the adsorbent is occurred and it is governed by molecular diffusion and by the eddy diffusion (Jørgensen et al., 2001):

$$\frac{dC_w}{dt} = k_c \left(C_w - C_{w.eq} \right) \qquad \text{(Eq.5.4)}$$

Where, K_c is external mass transfer coefficient (h^{-1}); C_w is initial concentration of PPCPs in liquid phase (ng/L); and $C_{w.eq}$ is concentration of PPCPs at the equilibrium in liquid phase (ng/L).

5.3 Results and discussion

5.3.1 Preliminary study on inhibition of bioactivity

Various methods for preventing bioactivity of microorganisms have been applied, such as sterilization by autoclave, addition of toxic substances and control of temperature. Although these methods are able to inhibit microbial activity, characteristics and complexity of sludge can be changed by causing negative effects on their activity from decay and transformation, and cells of sludge which provide new adsorption points may be damaged as well. Some researchers found great performance of inactivity without causing any problems when NaN_3 was employed as interrupter (Li et al., 2010; Yu et al., 2011). Consequently, to differentiate removal by biodegradation and adsorption NaN_3 was used in this experiment, in which inhibition of bioactivity was evaluated according to different concentrations of NaN_3 for selecting appropriate concentrations.

Since microorganisms utilize organic substrate like NH_3-N and readily biodegradable COD for growth and endogenous respiration, the variations of NH_3-N and $SCOD_{cr}$ concentration were observed to investigate the effect of NaN_3 and these results are shown in Figure 5.1 and Table 5.2, respectively. In the experiment of NH_3-N concentration, the concentration rapidly decreased in earlier period and above 90% was removed after 24 h without NaN_3, for instance, the consumed amount of NH_3-N was used for energy generation in the nitrification process and for the heterotrophic bacteria growth as nitrogen source, suggesting that combination of diversified MBR sludge and abundant aeration in the absence of NaN_3 can provide favorable condition for biodegradation. Also, as 0.1% of NaN_3 was added, gradual attenuation over time was found and about 50% of NH_3-N concentration was eliminated. While, although it was found to be slightly higher in 90 h than initial concentration, significant differences between 0 h and 90 h was not obtained in 0.5% and 1% NaN_3, showing that NaN_3 concentration of above 0.5% was necessarily required to inhibit microbial activity. It is true that comparing effect on bioactivity by concentration of NaN_3 is quite difficult due to the complexity of sludge composition and diversity, but our results were similar to other

reviews. Mozioti et al. (2015) reported that inactivation of microbial activity was achieved with 0.2% NaN_3, and a maximum state of inhibition of the microorganisms respiration was obtained after addition of NaN_3 for concentrations ≥0.2 g/g_{TSS} (Barbot et al., 2010), which was comparable to our experimental condition. Similar tendency was shown in variations of $SCOD_{cr}$ concentration, in which samples at 0 h and 90 h were analyzed and removal efficiencies were found to be 70% and 42%, respectively. While, insignificant difference between 0 h and 90 h was observed as above 0.5% NaN3 concentration was injected. Also, initial $SCOD_{cr}$ concentrations in 1% and 2% of NaN_3 were 2 times higher than other studied condition, which is likely due to release of intracellular substances and cell rupture by excess quantity.

From the results of water quality analysis, we certainly identified that 0.5% of NaN_3 was needed to interrupt activity and respiration of microorganisms, and thus it was selected as optimum concentration to conduct further batch experiments.

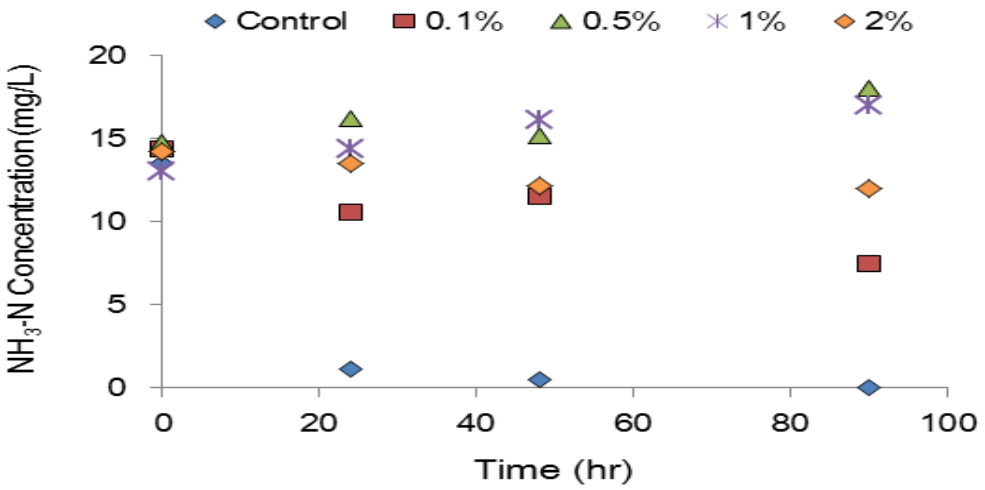


Figure 5.1 Variation of NH_3-N concentrations as a function of NaN_3 concentration

Table 5.2 Variation of $SCOD_{cr}$ concentration as a function of NaN_3 concentration

	Concentration of NaN_3 (w/v)				
	Control	0.1%	0.5%	1%	2%
$SCOD_{cr}$ concentration at 0 h (mg/L)	225	261	244	418	471
$SCOD_{cr}$ concentration at 90 h (mg/L)	68	151	251	444	451
Removal efficiency (%)	70	42	-3	-6	4

5.3.2 Comparison of zero, first and second-order kinetics

Before model discrimination is applied, the goodness of fit should be judged to represent estimated parameters. Therefore, the correlation between zero, first and second-order kinetics and the biodegradation data evaluated. Estimated parameters including rate constants and R-squared values are also summarized in Table 5.3.

Table 5.3 Parameters of zero, first and second-order kinetics

	Zero-order		First-order		Second-order	
	K_0	R^2	K_1	R^2	K_2	R^2
	μg/L·h		h^{-1}		L/μg·h	
Furosemide	5.0	0.96	0.205	0.99	1.2E-02	0.92
Naproxen	4.3	0.92	0.187	0.99	1.1E-02	0.98
Indometacin	0.6	0.91	0.051	0.99	6.1E-03	0.99
Diclofenac	0.4	0.98	0.049	0.98	8.8E-03	0.84
Griseofulvin	0.4	0.96	0.012	0.98	4.5E-04	0.96
Clofibric_acid	0.5	0.96	0.011	0.98	2.5E-04	0.96
Sulfathiazole	0.7	0.82	0.033	0.97	2.4E-03	0.91
Sulfamethoxazole	0.6	0.88	0.022	0.97	9.0E-04	0.99
Ketoprofen	5.3	0.85	0.258	0.96	2.1E-02	0.98
2QCA	0.7	0.99	0.018	0.94	5.5E-04	0.84
Bezafibrate	4.1	0.99	0.245	0.94	2.4E-02	0.84
Sulfamonomethoxine	0.6	0.85	0.015	0.93	4.5E-04	0.98
Crotamiton	0.2	0.86	0.004	0.87	4.9E-05	0.89
DEET	1.0	0.96	0.043	0.84	2.0E-03	0.67
Sulfapyridine	0.4	0.78	0.013	0.84	4.1E-04	0.83
Cyclophosphamide	0.1	0.83	0.001	0.83	1.9E-05	0.84
Trimethoprim	0.3	0.82	0.020	0.80	1.6E-03	0.73
Azithromycin	1.2	0.52	0.036	0.77	1.8E-03	0.65

With regard to linear relations between biodegradation and each kinetic model, they indicate the closer the value to 1, the higher the goodness of the fit. In all studied models, not only readily biodegradable compounds like naproxen, ketoprofen and bezafibrate, but also rarely biodegradable compounds like diclofenac and indomethacin showed a high goodness of fit regardless of rate constant. Unfortunately, biodegradation of all target compounds cannot be explained by these models because

there were some compounds which were not reacted by biodegradation, described as low R-squared value. Also, although the values were not enough higher to represent best fit, the values were ascertained to fit quite well with first-order kinetic model compared with zero and second-order kinetic models. Accordingly, rate constant by biodegradation can be described by first-order kinetic model in this batch study.

5.3.3 Classification of target compounds

In batch study, total 45 target compounds were analyzed and the effect of hydrolysis and volatilization was evaluated based on the experiments of R3 and R4, respectively, as can be seen in Table 5.4. In the same with removal of organic pollutants, some PPCPs may be eliminated by contributions of hydrolysis and volatilization, and particularly volatilization might be occurred in some compounds with a relative high Henry coefficient because MBR process is operated as conditions under typically higher aeration to alleviate membrane fouling by effect of stripping. However, average ratio ranged from 0.9 to 1.1, which means that no obvious changes on ratio of initial concentration and concentration at each sampling event were revealed in R4 and these values were certainly verified by coefficient of variations and 95% confidence intervals.

Also, with respect to volatilization the variation of concentrations were studied during 48 h, in which all target compounds were found to be stable and no differences between initial concentration and concentrations during the testing period were observed. It can be explained by the reasons that firstly, although volatilization can be significantly achieved in the compounds having Henry coefficient higher than 10^{-3}, it was not obtained due to Henry coefficient smaller than 10^{-5} in studied compounds and secondly, these compounds were characterized by relative high molecular weight and polarized functional groups. In our study, the effect of hydrolysis and volatilization were not relevant with removal of PPCPs and thus these contributions were ignored in differentiating the removal pathways, which were considerably consistent with recent reviews (Sipma et al., 2010; Li et al., 2010; Wang., 2013) in which they reported that hydrolysis and volatilization on removal of PPCPs could generally be assumed to be negligible. Consequently, compared with former two removal routes, biodegradation and adsorption processes are considered the most important mechanisms and target compounds were classified by suitable kinetic models into individual categories. Estimated model parameters including each rate constant, half-lives, R-squared values are summarized in detail, as can be seen in Table 5.5.

Table 5.4 Ratio of concentration on hydrolysis and volatilization

	Hydrolysis Ratio of C_t/C_0 (from 0 to 72 h)			Volatilization Ratio of C_t/C_0 (from 0 to 48 h)		
	Avg.	CV.	95% CI	Avg.	CV.	95% CI
Antipyrine	0.99	7%	4%	0.99	4%	3%
Ketoprofen	1.01	3%	2%	1.03	3%	2%
Naproxen	0.95	4%	3%	1.00	6%	5%
Fenoprofen	0.98	6%	4%	0.99	5%	4%
Diclofenac	1.00	4%	3%	1.00	4%	3%
Indometacin	0.97	5%	3%	0.98	5%	4%
Mefenamic_acid	1.00	4%	2%	1.01	4%	3%
Azithromycin	0.99	4%	3%	0.98	3%	2%
Tylosin	0.98	5%	3%	0.98	4%	4%
Clarithromycin	1.02	6%	4%	1.00	5%	4%
Roxithromycin	0.98	4%	3%	1.01	6%	5%
Tetracycline	0.96	7%	4%	1.03	4%	3%
Oxytetracycline	0.99	5%	3%	1.02	6%	5%
Thiamphenicol	1.06	5%	4%	1.02	5%	4%
Trimethoprim	0.97	4%	2%	0.97	4%	3%
Tiamulin	0.97	5%	3%	0.94	5%	4%
Sulfathiazole	1.04	3%	2%	1.01	4%	3%
Sulfapyridine	1.03	3%	2%	1.04	5%	4%
Sulfamerazine	1.02	2%	1%	1.03	5%	4%
Sulfadimidine	<LOQ			<LOQ		
Sulfamethoxazole	1.01	3%	2%	1.04	4%	3%
Sulfamonomethoxine	1.04	4%	2%	0.99	4%	3%
Sulfadimethoxine	0.96	3%	2%	0.98	4%	3%
Levofloxacin	0.98	2%	2%	1.02	5%	4%
Norfloxacin	0.98	5%	3%	0.96	3%	2%
Ciprofloxacin	0.94	4%	3%	0.96	7%	5%
Atenolol	1.00	3%	2%	1.03	4%	3%
Metoprolol	0.98	5%	3%	0.99	5%	4%
Disopyramide	0.98	4%	3%	0.94	4%	3%
Propranolol	0.96	4%	2%	1.00	4%	3%
Diltiazem	1.06	6%	4%	0.99	7%	6%
Clofibric_acid	0.96	3%	2%	1.04	4%	3%
Bezafibrate	0.99	5%	3%	1.04	4%	3%
Theophylline	1.00	5%	4%	1.02	2%	2%
Caffeine	1.03	4%	2%	1.03	3%	2%
Furosemide	1.00	6%	4%	1.00	4%	3%
DEET	0.94	6%	4%	1.05	5%	4%
2QCA	1.01	3%	2%	1.01	7%	6%
Primidone	1.02	2%	2%	1.03	5%	4%
Cyclophosphamide	1.00	3%	2%	1.04	3%	3%
Carbamazepine	1.07	6%	4%	0.95	5%	4%
Isopropylantipyrine	1.01	5%	3%	0.98	4%	3%
Griseofulvin	1.02	2%	1%	0.94	4%	3%
Crotamiton	0.92	6%	4%	1.00	4%	3%
Pirenzepine	0.98	3%	2%	1.02	7%	6%

Avg.: Average ratio, CV.: Coefficient of variation, 95% CI: 95% confidence interval and <LOQ: Limit of quantification.

NSAIDs

With the exception of antipyrine and fenoprofen, removal of NSAIDs was deeply related with biodegradation rather than adsorption and simultaneous kinetic models from the results of R-squared values. Naproxen was the compounds with the highest biodegradation constant (1.231 $L/g_{VSS}·d$), with removal efficiency showing above 95% after 5 h, which was in good agreement with previous study by Fernandez-Fontaina et al. (2013), who reported higher biodegradation kinetic constant of 0.5-4.2 $L/g_{VSS}·d$. Similarly, ketoprofen also was rapidly reacted with MBR sludge within 10 h, with biodegradation constant (0.587 $L/g_{VSS}·d$). Some studies suggested that ketoprofen was commonly removed via biodegradation, while sorption and volatilization seemed to be negligible, which was consistent with our results (Joss et al., 2006; Salgado et al., 2012). In addition to two compounds, R-squared values of other NSAIDs, such as diclofenac, indometacin and mefenamic acid, were found to be higher in biodegradation kinetic models. Although biodegradation constants were not very high, biodegradation of these compounds followed first-order kinetics, with half-lives ranging from 15.8 h and 31.3 h.

Moreover, it was demonstrated that adsorption equilibrium was reached after 10 h from K_d values obtained in our study. Similar reviews were reported by Parker et al. (1994), in which adsorption was generally assumed instantaneous, considering that adsorption was more rapid than biodegradation in typical HRT of activated sludge process (6-24 h). Therefore, effect of adsorption was compared using the K_d values after 10 h, in which some compounds like naproxen and ketoprofen, showing higher biodegradation constant than other NSAIDs, had lower K_d values (24.9 and 24.5 L/kg), which indicates significant contribution of biodegradation can be proven with low tendency of adsorption. Among NSAIDs groups, fenoprofen solely followed simultaneous removal kinetic and showed much faster elimination, with k_{bio} value of 3.435 $L/g_{VSS}·d$. K_d value of fenoprofen was not high, but normalized K_c value of 0.064 $L/g_{VSS}·d$ was determined, suggesting that removal of fenoprofen was attributed to initial mass transfer as well as biodegradation in despite of low adsorption tendency. While, in comparison to the readily biodegradable compounds, adsorption tendency of diclofenac, indometacin and mefenamic acid were found to be high, with K_d values of 66.3, 77.1 and 120 L/kg. However, no attenuation of concentration in liquid phase was observed in experiment of R2 so that adsorption rate could not be determined.

Antibiotics

Macrolide antibiotics such as azithromycin, tylosin, clarithromycin and roxithromycin fitted to simultaneous kinetic models well with R-squared values (above 0.95) and showed k_{bio} values from 0.103 to 0.138 $L/g_{VSS}\cdot d$, with half-lives ranging from 17.2 to 32.8 h, even though the k_{bio} values were not much higher than those of NSAIDs. It means that removal of macrolide antibiotics was attributed to both mass transfer of solute from liquid phase to the boundary layer of sludge and biodegradation. Reaction of these compounds was not described by only biodegradation kinetic model, in which each removal pathway could not be calculated from experiments of R1 and R2 because initial concentration of these compounds in solid phase was very high, which is caused by MBR sludge containing large amount of PPCPs. Moreover, K_d values had 59.1, 112.9, 62.2, and 56.8 L/kg in azithromycin, tylosin, clarithromycin and roxithromycin, which were not much higher than tetracycline antibiotics. Although our results were rather different from review by Göbel et al. (2005), who demonstrated that 10 times higher K_d values in azithromycin (380 L/kg) and clarithromycin (260 L/kg), adsorption rate was certainly expressed by external mass transfer constant, K_c values, with R-squared values (0.86-0.99).

For tetracycline antibiotics, they adsorbed rapidly onto MBR sludge with low biodegradability, which was accounted for by the results of significant k_d values of tetracycline (9167.9 L/kg) and oxytetracycline (8707.6 L/kg). Batt et al. (2007) reported that removal of tetracycline was positively affected to the adsorption. Also, concentration of trimethoprim, is an antibiotic used mainly in the treatment of bladder infections, was not changed during the experiment period, indicating that removal of this compound was not relevant with biodegradation and adsorption tendency and thus it is not expected to eliminate efficiently in MBR process. This was in agreement with the results of a few studies which summarized that biodegradation of trimethoprim was quite low than other antibiotics, with K_{bio} value ranging from 0.05 to 0.09 (Abeggle et al., 2009). According to Pérez et al. (2005), trimethoprim displayed high resistance to microbial degradation in the sewage from activated sludge treatment. Also, removal of tiamulin was ascertained to fit quite well with simultaneous kinetic model compared with biodegradation kinetic model, for which high adsorption tendency was observed, but k_{bio} value was found to be 0.075 $L/g_{VSS}\cdot d$, showing the low biodegradability.

Sulfonamide antibacterials

In general, regarding MBR sludge, high adsorption affinity is obtained by increased specific surface area originated from smaller particle size which was developed in

MBR operation. However, sulfonamide antibacterials showed the lowest adsorption tendency, with average K_d values less than 30 L/kg. Even though these compounds fitted to simultaneous kinetic model except for sulfapyridine and sulfadimethoxine, they were hardly biodegraded with MBR sludge in spite of their hydrophilic properties, which showed very low k_{bio} values (below 0.01 $L/g_{VSS}\cdot d$) with long half-lives. Sulfathiazole was solely removed up to 80% in the end of the experiments and it showed relatively higher k_{bio} value than other sulfonamide compounds, indicating that enough time is necessary for this compound to be biologically degraded, but it can be eliminated in MBR process operated by long SRT. These results were in accordance with recent reviews that sulfamethoxazole was rarely biodegraded with MBR biomass (0.10-0.30 $L/g_{VSS}\cdot d$) (Fernandez-Fontaina et al., 2013), in another work, Abegglen et al. (2009) also reported that some sulfonamide antibacterials were fairly well biodegraded and hardly adsorbed to the sludge, with biodegradation constant of 0.19 $L/g_{VSS}\cdot d$ in sulfamethoxazole.

Fluoroquinolone antibacterials

With regard to the fate of fluoroquinolone antibacterials, mass transfer was rapidly observed from liquid phase to solid phase, leading to non-linear reactions (as measured low R-squared values) due to insufficiency of concentrations remaining in liquid phase. Thus, these compounds could not be estimated by three kinetic models and only adsorption tendency was evaluated using the K_d values. The adsorption equilibrium was reached within 1 h, indicating the removal was dominated by adsorption. Estimated K_d values of levofloxacin, norfloxacin, ciprofloxacin and enrofloxacin had 5,530, 5,918, 6,906, and 3,702 L/kg, respectively. Fluoroquinolone antibacterials have been reported as the compounds which were highly adsorbed onto sludge phase and the results obtained in our field survey of Chapter III confirmed this behavior. For instance, significantly higher values were observed for ciprofloxacin and norfloxacin, with K_d values of 20,000 and 15,850 kg/L, respectively (Golet et al., 2003). Narumiya et al. (2013) studied PPCPs adsorbed onto primary sludge and excess sludge in activated sludge process, in which maximum k_d values of ciprofloxacin and levofloxacin were 1,896 and 6,706 kg/L.

It is known as compounds with a high K_{ow} value have more affinity for the solid fraction, but the log K_{ow} values of them ranges from -0.39 to 0.7, as can be seen in Table 2.1, which is insufficient to achieve hydrophobicity. Therefore, high adsorption tendency of fluoroquinolone antibacterials can be explained by the electrostatic

interactions between the compounds and sludge rather than their hydrophobicity, which was also identified by some researchers. They reported that adsorption of activated sludge or sediment was attributed to electrostatic interaction, surface complexation and hydrogen bridges rather than hydrophobicity (Tolls., 2001; Ternes et al., 2004). In fluoroquinolone compounds, it was difficult to elucidate the contribution of biodegradation and adsorption through our designed batch test, so other alternatives should be considered by adjusting MLSS concentration and conducting the experiment under continuous operation to determine reactions by immediate transfer.

Antiarrhythmic agents

Among antiarrhythmic agents, removal of diltiazem and two beta blockers such as atenolol and metoprolol showed a high goodness of fit in terms of simultaneous kinetic model. Although it was apparent that atenolol concentration in solid phase was not available due to low recovery rate and bioactivity was not inhibited in spite of addition of NaN_3, the concentration in liquid phase was found to be rapidly attenuated up to 94% within 5 h, suggesting that removal of this compound was positively related with biodegradation. There have been several conflicting reports on removal routes of beta blockers. According to a study by Wang et al. (2013), the strong adsorption affinity of atenolol could be explained by its positive charge, as the sludge exhibited a negative charge, the electrostatic attraction made the adsorption process stronger than other routes. On the other hand, Sathyamoorthy et al. (2013) highlighted that impact on biodegradation and cometabolism in eliminating beta blockers like atenolol and metoprolol, in which adsorption had a negligible influence on attenuation of concentration. Also, adsorption capability was not considerably obtained in atenolol, with K_d values ranging from 30 to 46 kg/L (Wick et al., 2009; Stevens-Garmon et al., 2011), being consistent with our results.

Besides, relative high adsorption tendency was observed in diltiazem and propranolol, with K_d values of 100 and 655 L/kg. The removal of diltiazem perfectly followed simultaneous kinetic (R-squared value: 0.99) as well as adsorption kinetic model (R-squared value: 0.99), in which 77% of initial concentration was eliminated after 96 h and particularly the highest mass transfer rate, with normalized K_c value of 0.2 $L/g_{VSS}\cdot d$ was obtained. It indicates that removal of diltiazem was dominant by mass transfer from initial period to 48 h while simultaneously improving degradation.

Others

In experiment of R2, inhibition of microbial activity with NaN_3 was not achieved in caffeine and theophylline similar to atenolol, but they had the highest biodegradation rate, with K_{bio} constant of 28.0 and 15.4 $L/g_{VSS}\cdot d$ using simultaneous kinetic model among all target PPCPs (both R^2 >0.99). These compounds were completely removed within 1hr, which was attributable to rapid decrease of their concentration in liquid phase, even though there was no adsorption affinity and normalized K_c values were not determined. It indicates that extremely high removal efficiency of these compounds obtained from our previous study in MBR process, with various biological treatment processes could certainly be explained by result of this study.

For biodegradation of DEET, 47% of initial concentration was removed at 72 h and removal efficiency reached to 77% after 96 h. Although higher biodegradation constant was obtained in simultaneous kinetic model than biodegradation kinetic model, R-squared values of biodegradation (R^2 >0.83) and adsorption kinetic models (R^2 >0.88) were higher than those of simultaneous kinetic model (R^2 >0.74), indicating that removal of DEET can be affected by each mechanism rather than by combination of biodegradation and adsorption. No data was found in literature to compare our results, but Xue et al. (2010) classified target compounds into two different patterns using mass balance and kinetic models, i.e.: biodegradation-dominating pattern and adsorption-biodegradation collaborating pattern. They concluded that removal of caffeine and DEET was related with the biodegradation-dominating pattern.

Since griseofulvin, belongs to the group of medicines called antifungals, has not been detected in WWTPs during several decades, it is not fully understood. Therefore, it is interesting to note that removal of this compound fitted to simultaneous kinetic model well with half-lives of 59.1 h and K_{bio} value of 0.036 $L/g_{VSS}\cdot d$, in which although R-squared value was not high, high adsorption velocity was observed. Similar to diltiazem, elimination of griseofulvin in MBR seems to be influenced by the collaboration of biodegradation and adsorption. The similar tendency was also shown in the removal of crotamiton which has been reported as recalcitrant compound in the field of wastewater treatment, although biodegradation rate and elapsed time to reach equilibrium of this compound was lower than that of griseofulvin. There is not sufficient information on removal fate and routes of some compounds, and consequently further study has to focus on the understanding the contributions of biodegradation and adsorption for frequently detected compounds in water environment as well as others which have not been extensively studied to achieve the highest removal performance.

Table 5.5 Model parameters of each compound

		Biodegradation kinetic model				Simultaneous kinetic model				Adsorption kinetic model			
		Rate constant	Half-lives	K_{bio}	R^2	Rate constant	Half-lives	K_{bio}	R^2	K_d (after 10 h)	K_c	Normalized K_c	R^2
		h^{-1}	h	$L/g_{VSS}\cdot d$		h^{-1}	h	$L/g_{VSS}\cdot d$		L/kg	h^{-1}	$L/g_{VSS}\cdot d$	
1	Antipyrine	< 0		0.003		< 0				23.5			
2	Ketoprofen	0.280	2.5	0.587	0.91	0.088	7.9	0.230	0.84	24.5			
3	Naproxen	0.587	1.2	1.231	0.92	0.718	1.0	1.804	0.83	24.9			
4	Fenoprofen	0.063	11.1	0.131	0.86	1.228	0.6	3.435	0.99	36.8	0.030	0.064	0.96
5	Diclofenac	0.022	31.3	0.046	0.90	0.010	71.2	0.032	0.97	66.3			
6	Indometacin	0.033	20.9	0.069	0.93	0.007	105.9	0.021	0.90	77.1			
7	Mefenamic_acid	0.044	15.8	0.092	0.97	0.008	89.9	0.038	0.96	120.0			
8	Azithromycin	< 0				0.030	23.1	0.125	0.95	59.1	0.075	0.158	0.86
9	Tylosin	< 0				0.021	32.8	0.103	0.96	112.9	0.078	0.164	0.86
10	Clarithromycin	0.000	2508.3	0.001	0.01	0.037	18.5	0.132	0.98	62.2	0.046	0.096	0.99
11	Roxithromycin	0.001	1167.7	0.001	0.01	0.040	17.2	0.138	0.98	56.8	0.055	0.115	0.86
12	Tetracycline	0.003	231.6	0.006	0.60	0.002	311.6	0.494	0.58	9167.9			
13	Oxytetracycline	0.006	117.2	0.012	0.72	< 0				8707.6			
14	Thiamphenicol	<LOQ				0.010	66.8	0.026	0.32	15.4			
15	Trimethoprim	< 0				0.001	647.1	0.004	0.13	71.7			
16	Tiamulin	< 0				0.010	69.8	0.075	0.96	259.1	0.042	0.087	0.69
17	Sulfathiazole	0.013	54.4	0.027	0.99	0.015	47.4	0.038	0.99	26.5			
18	Sulfapyridine	0.004	187.7	0.008	0.48	0.002	374.7	0.005	0.39	25.0	0.027	0.057	0.76
19	Sulfamerazine	0.005	129.8	0.011	0.93	0.003	269.7	0.007	0.92	22.3			
20	Sulfadimidine	< 0		0.000		< 0				62.9			
21	Sulfamethoxazole	0.007	96.1	0.015	0.93	0.004	156.4	0.011	0.96	16.7			
22	Sulfamonomethoxine	0.003	230.7	0.006	0.47	0.002	284.5	0.006	0.88	19.0			
23	Sulfadimethoxine	0.006	120.7	0.012	-	0.007	103.8	0.016	0.34	48.9			
24	Levofloxacin	<LOQ				0.001	489.9	0.083	0.59	5330.0			
25	Norfloxacin	<LOQ				0.001	634.9	0.157	0.47	5918.2			
26	Ciprofloxacin	<LOQ				0.001	1259.4	0.078	0.42	6906.3			
27	Atenolol	0.000	17678.4		0.27	0.272	2.5	-	0.94	<LOQ			
28	Metoprolol	0.008	90.1	0.016	0.95	0.008	83.5	0.023	0.98	32.9	0.049	0.103	0.09
29	Disopyramide	< 0				0.001	645.5	0.004	0.27	76.1			
30	Propranolol	0.005	126.2	0.012	0.23	0.004	162.7	0.071	0.74	655.3			
31	Diltiazem	< 0				0.016	44.0	0.074	0.99	99.9	0.097	0.202	0.99
32	Clofibric_acid	0.001	947.3	0.002	0.30	0.001	601.6	0.003	0.51	18.9			
33	Bezafibrate	0.284	2.4	0.595	0.46	0.813	0.9	2.070	0.74	26.2			
34	Theophylline	< 0				6.049	0.1	15.394	1.00	10.2			
35	Caffeine	< 0				5.513	0.1	27.979	1.00	13.2			
36	Furosemide	0.115	6.0	0.240	0.82	0.031	22.2	0.080	0.89	33.7			
37	DEET	0.016	44.6	0.033	0.83	0.041	17.0	0.109	0.74	26.3	0.022	0.045	0.88
38	2QCA	0.010	69.5	0.021	0.99	0.006	110.3	0.016	0.98	18.2			
39	Primidone	< 0				< 0				26.5			
40	Cyclophosphamide	< 0		0.001		< 0				21.4			
41	Carbamazepine	0.001	568.8	0.003	0.02	0.002	448.7	0.004	0.01	47.6			
42	Isopropylantipyrine	0.001	523.7	0.003	0.01	0.000	-	0.000	0.01	26.8			
43	Griseofulvin	0.006	123.9	0.012	0.86	0.012	59.1	0.036	0.98	54.4	0.112	0.236	0.83
44	Crotamiton	< 0				0.004	194.4	0.010	0.85	36.2	0.035	0.074	0.99
45	Pirenzepine	0.001	1140.9	0.001	-	0.001	564.5	0.004	0.17	39.7			

5.3.4 Comparison of MBR and CAS

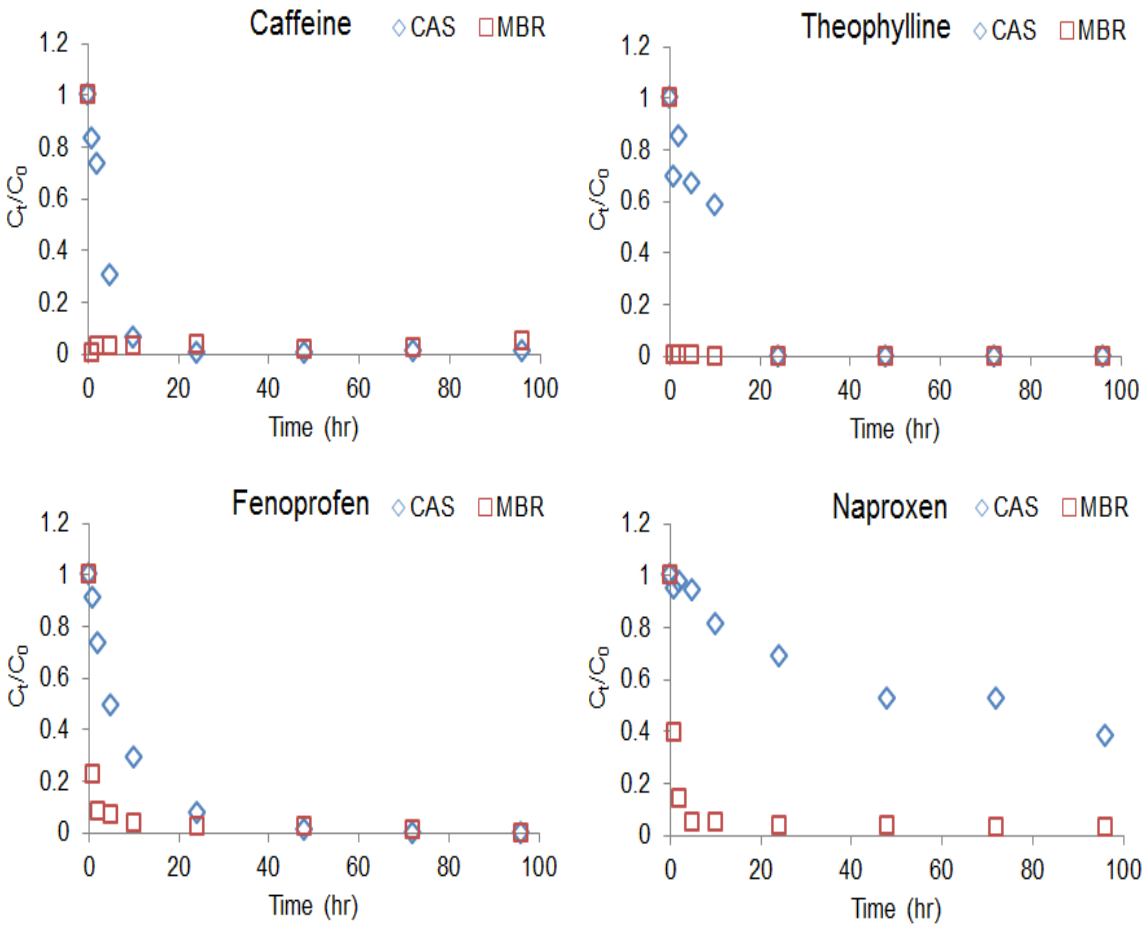
Several studies have been focused on investigation of elimination routes in MBR or CAS, but not only target compounds widely differ from individual to individual, but also specific experimental design such as sampling time, aeration intensity and initial concentrations of standard solution are considerably varied so that it is difficult to directly compare their removal pattern between results obtained from our study and literature values. Therefore, we carried out the batch test under the identical conditions except for sludge characteristics in order to elucidate the difference between the sludge developed in MBR and CAS process. The results including parameters of biodegradation and adsorption obtained from both experiments are summarized in Table S-1 of supporting information (henceforth SI).

High removal in MBR and high/moderate removal in CAS

As shown in Figure 5.2, caffeine and theophylline were highly biodegraded with both MBR and CAS sludge. In removal of CAS, significantly high biodegradation was obtained, with K_{bio} values of 6.4 and 9.8 $L/g_{VSS}\cdot d$ in caffeine and theophylline, and even higher K_{bio} values were shown in MBR sludge (caffeine: 28.0 $L/g_{VSS}\cdot d$ and theophylline: 15.4 $L/g_{VSS}\cdot d$), showing that these compounds can be completely removed in biological treatment process regardless of differences of biomass. Regarding the removal of fenoprofen, almost similar K_{bio} values were found in both types (3.4 $L/g_{VSS}\cdot d$ in MBR and 2.8 $L/g_{VSS}\cdot d$ in CAS). Although MBR was superior to CAS sludge in terms of removal by simultaneous kinetic model, higher normalized K_c was obtained in CAS.

Also, removal by biodegradation of bezafibrate and NSAIDs like naproxen and ketoprofen showed a similar pattern in both types of sludge, but greater K_{bio} values were observed in MBR. The K_{bio} values of CAS were found to be 1.207, 0.284 and 0.229 $L/g_{VSS}\cdot d$ in bezafibrate, naproxen and ketoprofen, which increased to 2.070, 1.231 and 0.587 $L/g_{VSS}\cdot d$ in MBR. Half-lives of bezafibrate, naproxen and ketoprofen were greatly diminished from 16.8, 69.3 and 86.0 h in CAS to 0.9, 1.2 and 2.5 h in MBR. There is little consensus on the results of Joss et al. (2006), who reported K_{bio} values of 3.4-4.5 and 0.4-0.8 $L/g_{SS}\cdot d$ with MBR biomass in bezafibrate and naproxen, in which for removal of bezafibrate was achieved at a significantly higher rate in MBR compared to the CAS, while in case of naproxen, 2 times higher biodegradation rate was found in CAS. Judging from K_{bio} values and half-lives of both cases, it can be concluded that

these compounds will not be efficiently removed under typical HRT of CAS system operated at 10-20 h. Since the large amounts of these compounds have frequently been detected in WWTPs, much caution is required to handle them efficiently. Accordingly, enhanced biodegradation in MBR process can allow the compounds to be degraded in a few hours, leading to the efficient management in PPCPs removal. This tendency can be explained by following two reasons. Firstly, the higher MLSS concentration by long SRT may affect the overall biological activity of slow growing microorganisms such as nitrification, thereby resulting in significant biodegradation potential. Secondly, microbial diversity and the relative shortage in biodegradable organic matter in the condition of low F/M ratio may cause microorganisms to metabolize hardly degradable or recalcitrant compounds (Côté et al., 2004; Clara et al., 2005).



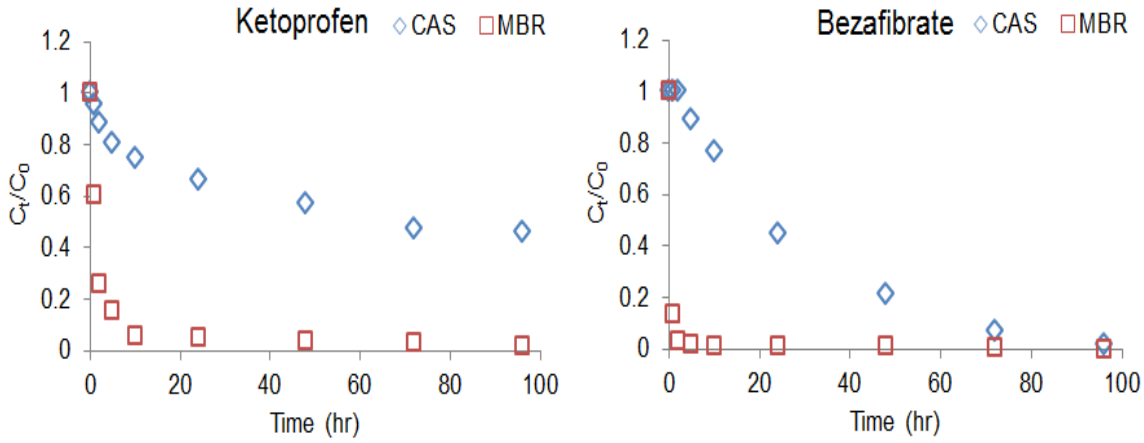


Figure 5.2 Changes of relative concentration of the compounds showing high removal in MBR and high/moderate removal in CAS

Moderate removal in MBR and poor removal in CAS

Regarding CAS sludge, furosemide and diclofenac were not biologically degraded and DEET was found to be poorly removed (Figure 5.3). In particular, for removal of diclofenac with MBR sludge, previous results of K_{bio} values were indicated by Fernandez-Fontaina et al. (2013), in which a very low biodegradability was found with less than 0.1 $L/g_{VSS}\cdot d$. Abegglen et al. (2009) also reported low value for diclofenac (less than 0.02 $L/g_{SS}\cdot d$). However, in our study, removals of these compounds were partially achieved in MBR, with 0.080, 0.046 and 0.109 $L/g_{VSS}\cdot d$ of K_{bio} values for furosemide, diclofenac and DEET, respectively. There were no significant differences on K_d value and adsorption constant between MBR and CAS, suggesting that increased removal performance of them was solely affected by biodegradation of MBR sludge. However, unlike furosemide and DEET, removal of diclofenac was continued during initial 48 h and was not completely achieved within designed time intervals, which can be partially suggested by our results in lab-scale MBR process, in which it was found to be rarely degraded in MBR process, with less than 40 % in biodegradation rate.

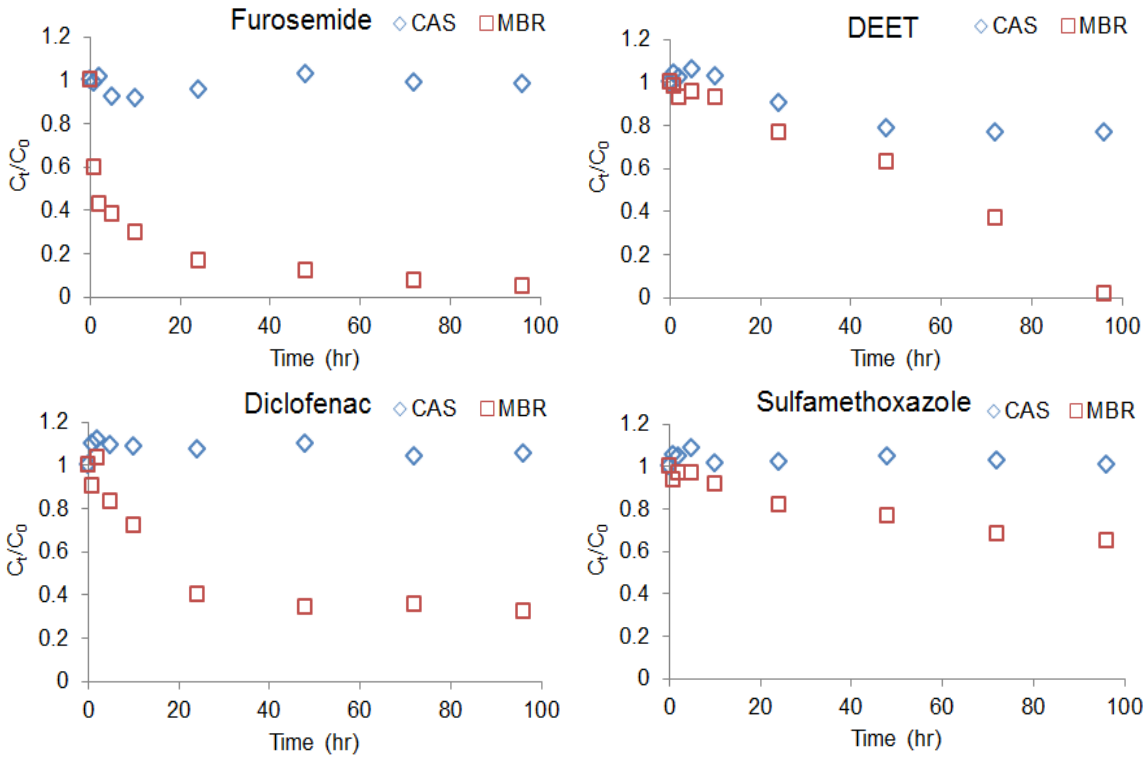
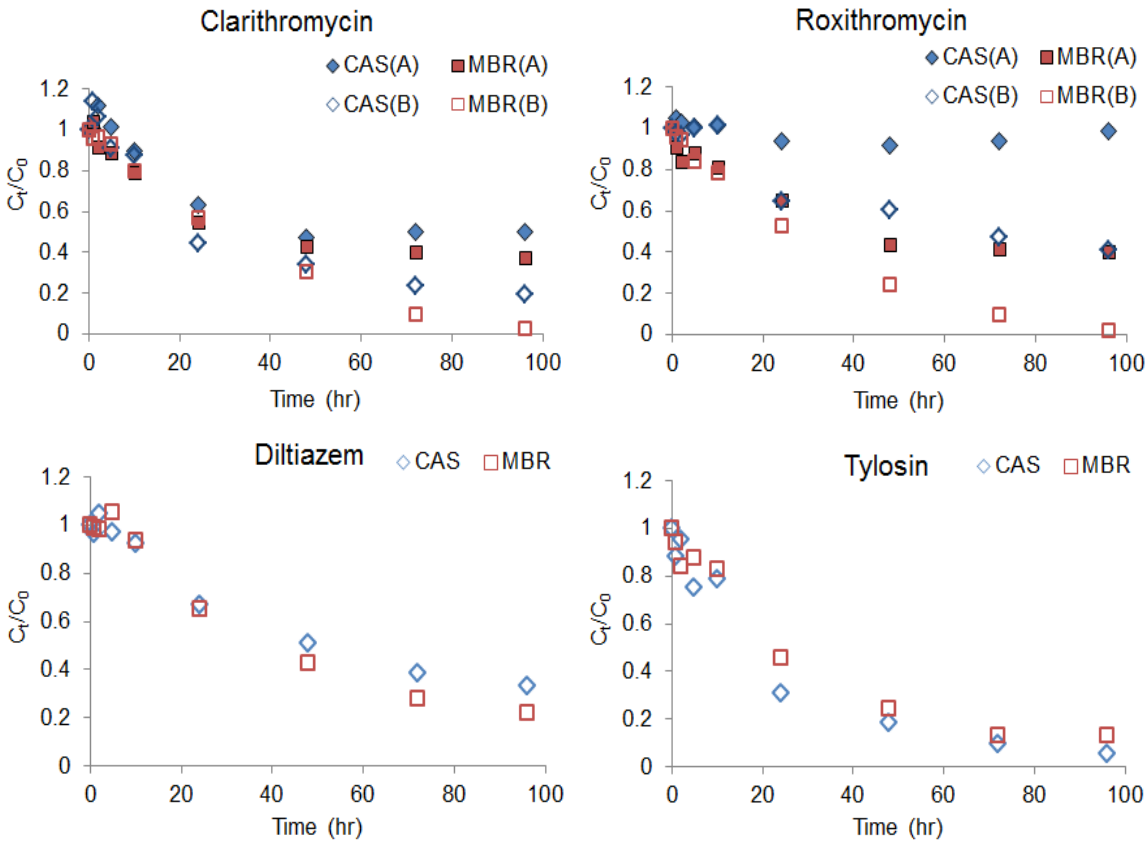


Figure 5.3 Changes of relative concentration of the compounds showing moderate removal in MBR and poor removal in CAS

With regard to sulfonamide antibacterials, no change of concentrations was obtained in CAS, but they were slowly degraded with MBR sludge, as can be shown in sulfamethoxazole of Figure 5.3. Also, contribution of adsorption was insignificant from the results of low K_d values because of intrinsic properties of these compounds having low log k_{ow} values (0.05-1.6). Similar tendency was also identified in the removal of sulfathiazole and sulfamerazine. According to Yang et al. (2012), they reported the fate of sulfonamide antibacterials in contact with activated sludge in which the removal of sulfonamides such as sulfamethoxazole, sulfadimethoxine and sulfamonomethoxine was achieved after initial lag phase of 2 d and it continued to decrease till complete disappearance (> 99% removal) at the end of 14 d. Although MBR sludge was more effective in degrading sulfonamide compounds than CAS sludge, biodegradation rate constant was extremely low in both types. Therefore, it can be assumed that removal fate of these compounds are affected by enough contact time between sludge and compounds for biodegradation rather than sludge characteristics described by sludge age, type and concentration. In order to make sure this assumption, further study is necessarily required by extending the experimental period.

High K_{bio} values in CAS than MBR

Although the first-order rate constant is an apparent value to indicate the biodegradation rate of PPCPs in MBR and CAS, it is very difficult to compare biodegradation capability of biomass provided from different types, and thus normalized K_{bio} value by the MLVSS concentration and K_d value was applied. For macrolide antibiotics clarithromycin and roxithromycin showed higher first-order rate constant in MBR (0.037 and 0.040 h^{-1}, respectively) than in CAS (0.017 and 0.009 h^{-1}, respectively). K_{bio} values, however, was greater in CAS (0.522 and 0.280 $L/g_{VSS}\cdot d$ in clarithromycin and roxithromycin, respectively) than in MBR (0.132 and 0.138 $L/g_{VSS}\cdot d$, respectively), even though MBR was more effective in eliminating these compounds as can be seen in Figure 5.4. This pattern was also shown in the removal of diltiazem, where K_{bio} value was found to be 5 times higher in CAS while half-lives and first-order constant were low in CAS. Compared with K_{bio} values of MBR obtained in our study and other literature reviews, relatively higher values from CAS sludge was due to over 10 times greater MLVSS concentration in MBR (11,450 mg/L) than in CAS (845 mg/L).



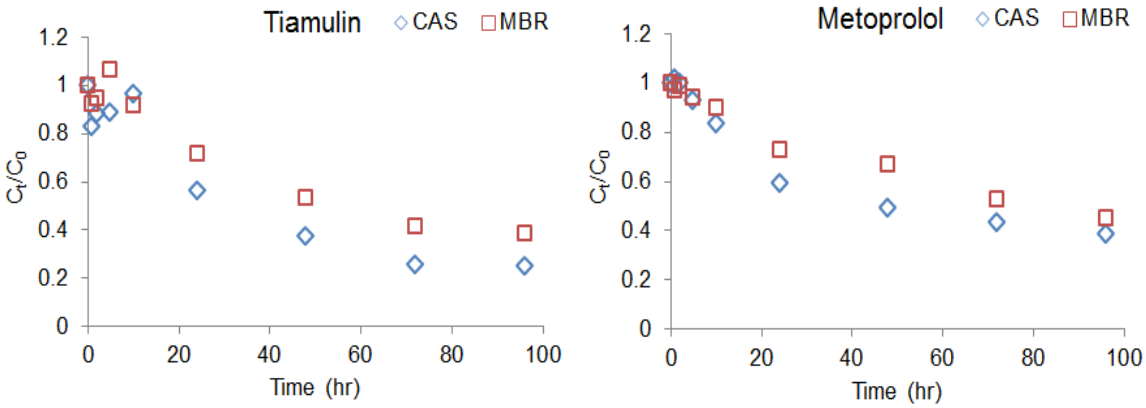


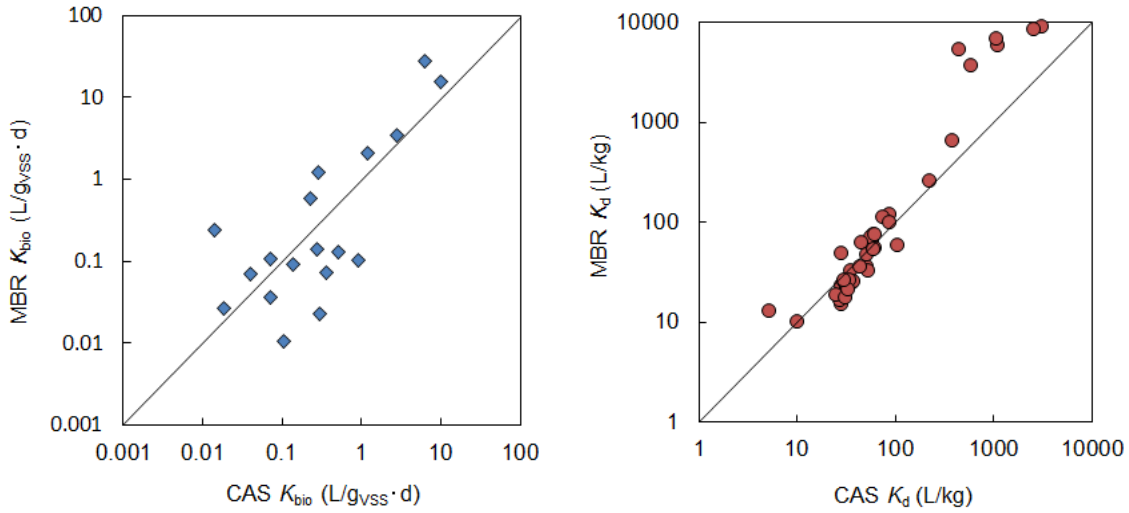
Figure 5.4 Changes of relative concentration of the compounds showing higher K_{bio} values in CAS than MBR

On the other hand, some substances such as tylosin, tiamulin and metoprolol showed higher K_{bio} values in CAS, with 0.931, 0.519 and 0.293 L/g_{VSS}·d of K_{bio} values which were about 10 times greater than those in MBR, as well as changes of relative concentration of these compounds were quickly achieved in CAS as can be seen in Table S-1 of SI. Therefore, as against the removal of clarithromycin, roxithromycin and diltiazem higher K_{bio} values of these compounds cannot be merely explained by increased MLSS concentration attributed to MBR process. Although it was found to be lower K_d values in CAS, normalized K_c values of tylosin and tiamulin increased from 0.164 and 0.087 L/g_{VSS}·d in MBR to 2.694 and 1.131 L/g_{VSS}·d in CAS. The removal of these compounds followed simultaneous kinetics, in which they were affected by both biodegradation and enhanced mass transfer rate. Similarly, Joss et al. (2006) reported that as SRT increased inert particulate matter was accumulated in reactor and thus relative fraction of heterotrophic bacteria in MBR was reduced to about twice in comparison to CAS sludge. However, it cannot be described completely for fate of all target compounds since these patterns were only shown in above some substances, thereby requiring further research on increased biodegradability found in CAS compared with MBR process.

Comparison of K_{bio} and K_d values observed with MBR and CAS sludge

Fig. 5.5 (a) gives an overview of biodegradation kinetic constant obtained from biodegradation and simultaneous kinetic models between MBR and CAS sludge, in which hardly degradable compounds during designed experiments such as sulfonamide and fluoroquinolone antibacterials could not be represented by both

kinetic models due to discrepancy of mass balance in comparative study. Also, target compounds are classified into four groups according to the range of K_{bio} values (Table 5.6).



(a) K_{bio} value (b) K_d value

Figure 5.5 Comparison of K_{bio} and K_d values between MBR and CAS

Table 5.6 Summary of target compounds according to the range of K_{bio} values

Conditions	Compounds
Very highly biodegradable (10 < K_{bio} value) → MBR > CAS	CAF, TEP
Highly biodegradable (1 < K_{bio} value < 10) → MBR ≫ CAS	FP, BZF, NPX, KTP (<0.6)
Moderately biodegradable (0.1 < K_{bio} value < 1) → MBR ≦ CAS	TYL, CAM, RXM, MFA, DTZ, CRT, MPL, TL
Hardly biodegradable (0.01 < K_{bio} value < 0.1) → MBR > CAS	DCF, AZM, IND, FSM STZ, DEET

Some compound like caffeine, theophylline, fenoprofen, bezafibrate and naproxen, having above 1 L/g_{VSS}·d K_{bio} values in CAS were much highly degraded in MBR, suggesting that MBR sludge had a beneficial effect on removal of PPCPs by enhancing biodegradability. Also, moderately biodegradable compounds with K_{bio} values ranging from 0.1 to 1 L/g_{VSS}·d in CAS were found to be lower values in MBR (0.01< K_{bio} values < 0.1 L/g_{VSS}·d). This pattern was shown in the compounds which

more tend to adsorb onto sludge such as macrolide antibiotics. It appeared that the lower biodegradability observed in MBR was attributable to 10 times higher MLVSS concentration in MBR process for clarithromycin, roxithromycin and diltiazem. Regarding hardly biodegradable compounds, such as diclofenac, indometacin, sulfathiazole and DEET, the fate of persistent or non-degradable characteristics in CAS moved from a recalcitrant behavior to a partial removal in MBR sludge ($0.01 < K_{bio}$ value < 0.1 L/g_{VSS}·d). It might be related with long SRT which can facilitate elimination of hardly biodegraded compounds in promoting adaption of diverse bacteria and slow growing species.

Moreover, with regard to adsorption capability, K_d values of tetracycline and fluoroquinolone compounds, ranging from 442.6 to 3051.5 L/kg in CAS, significantly increased to 3702.6 to 9167.9 L/kg in MBR, which showed 3-10 times higher values (Figure 5.5 (b)), which was somewhat lower than results of our field and lab-scale studies (Figure 3.9), but stronger adsorption affinity to sludge in MBR could be identified. Interestingly, in addition to some adsorptive PPCPs, there were no significant differences on K_d and normalized K_c values of most studied compounds between MBR and CAS biomass, showing that adsorption tendency and mass transfer rate were not significantly relevant with sludge characteristics. Partition of target compounds and the adsorption propensity were attributed to the intrinsic nature of each substance rather than the sludge characteristics and conditions.

5.4 Conclusions

Through this batch study biodegradation and adsorption constants of target compounds were successfully determined with MBR sludge by applying different kinetic models, in which they were categorized according to removal characteristics and pathways. Also, comparative evaluation between sludge of different types (MBR versus CAS) was performed with model parameters such as reaction constant, half-lives and normalized K_{bio} values. This chapter summarizes major conclusions as can be seen below.

1) From the preliminary study, bioactivity of microorganisms was inhibited with the concentration of 0.5 % NaN_3. Since removal of PPCPs was not attributable to hydrolysis and volatilization, elimination via these mechanisms was considered negligible.

2) Removal pathways of individual compounds were significantly relevant to classes and categories of PPCPs. Caffeine and theophylline fitted simultaneous removal kinetic well, and the removal of most NSAIDs followed biodegradation kinetic model, in which significantly higher biodegradation rate was observed with MBR sludge.

3) For macrolide antibiotics higher goodness of fit was observed in simultaneous removal kinetic which means that mass transfer of solute from liquid to the boundary layer of sludge and biodegradation were simultaneously occurred. In contrast, concentration of tetracycline compounds was not detected in liquid phase due to rapid initial adsorption tendency and thus non-linear reactions were identified.

4) From the results of comparative evaluation between MBR and CAS, the fate of persistent or non-degradable substances like furosemide, diclofenac, sulfathiazole and DEET in CAS sludge moved from a recalcitrant behavior to a partial removal in MBR sludge, which can be attributed to enhanced biodegradation.

5) Removal of PPCPs showing very high or high biodegradable characteristics was greatly achieved via biodegradation in MBR compared with CAS. However, some compounds which more tend to adsorb to sludge, with K_{bio} values ranging from 0.1 to 1 $L/g_{VSS}.d$ were found to be higher values in CAS.

6) No obvious differences on adsorption affinity and mass transfer rate of most PPCPs between MBR and CAS sludge were observed, suggesting that removal via adsorption was not strongly dependent on the sludge characteristics. Thus, MBR process is not expected to outcompete the CAS process in terms of removal by adsorption despite high MLSS concentration.

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ChapterⅥ

Understanding the Effect of Microbial Diversity and Composition

6.1 Introduction

In the last two decades, MBR process has been widely applied for treatment of domestic and industrial wastewater. It has been known that MBR can offer several merits over other kinds of biological treatment processes in removing trace organic substances like PPCPs and EDCs as well as conventional organic pollutants and nutrients (Kimura et al., 2005; Terzic et al., 2005; Bernhard et al., 2006; Hu et al., 2007; Miège et al., 2009; Sipma et al., 2010). Although biodegradation of easily biodegradable contaminants like ibuprofen, caffeine, galaxolide and methylparaben can be efficiently obtained in even CAS system (Oppenheimer et al., 2007; Roh et al., 2009; Tran et al., 2009), more rapid and complete attenuation of most PPCPs can be achieved in MBR due to primarily enhanced biodegradability, which was also obviously proven by results of our batch experiments as mentioned in Chapter V.

In MBR process, higher MLSS concentration derived from increased SRT is able to promote microbial activity and diversity, thereby resulting in enhancement of biodegradation potential. Some reports demonstrated greater attenuation of PPCPs concentration with longer SRT (Kreuzinger et al., 2004; Joss et al., 2006). Moreover, slow growing bacteria like autotrophic nitrifiers (e.g., AOB and nitrite oxidizing bacteria (NOB)) can be enriched with increased microbial diversity caused by high SRT, which allow them cometabolise a large variety of PPCPs via the non-specific enzymes, such as AMO (Kocamemi et al., 2010; Helbling et al., 2012; Tran et al., 2013). Fernandez-Fontaina et al. (2012) proved that biotransformation of PPCPs was correlated to nitrification rate, assuming limitations in kinetics, energy and electron flows

caused by primary substrate degradation. Also, it has been highlighted that SRT in biological treatment systems can affect directly on the biomass composition by changing ratio between autotrophic and heterotrophic bacteria. According to a review by Xia et al. (2012), specific bacteria became the dominant species in activated sludge treatment process under conditions of longer SRT, which can play a key role in cometabolic biodegradation in WWTP in terms of biodegradation of antibiotic substances.

However, there are only a few studies on the effects of biodegradability according to variation of MLSS concentration (i.e., longer SRT), and ever fewer reviews on the knowledge of autotrophic bacteria like AOB and NOB, which can actually control the biodegradation by cometabolism in terms of PPCPs removal.

Based on the available literatures and previous batch experiments, it can be assumed that target compounds, showing higher biodegradation in MBR, are closely linked to effect of either microbial diversity or change of composition. In this chapter, therefore, we identified the influences of slow growing bacteria in removal of PPCPs and the presence of more diverse microbial communities with broader physiological capabilities through designed batch tests. Also, the role of microbial composition and influence of their relevant enzymes were studied by assessing the correlations between biodegradation of PPCPs and ammonia oxidation activity. Through these results they can be used as model parameters for predicting removal performance and characteristics of target compounds, which will be discussed in following chapter in more detail.

6.2 Materials and methods

6.2.1 Experimental design

6.2.1.1 Experiment on variation of SRT

Each target compound was investigated using separate sets of batch experiments to evaluate removal by variations of SRT and experimental design are summarized in Table 6.1. Six 500 mL flasks with 400 mL MBR sludge were simultaneously run at 25 ℃ with pH ranged from 6.7 to 7.5 and constantly agitated on a shaking plate at 100 rpm. MBR sludge was collected from pilot-scale MBR plant located in K (R1) and O (R2 and

R3) city of Japan, operating 8,380, 14,340 and 21,800 mg/L of MLSS concentration with different SRT of 18, 30 and 60 d in R1 and R2 and R3, respectively. Standard solution was spiked as final concentration of 100 μg/L and 0.5% of NaN_3 was used to inhibit the activity of microorganisms. Amber flasks were used to avoid possible photodegradation and inflow of DO was maintained above 4 mg/L during all times after sludge addition. 15 mL of each sample was collected at intervals of 0, 1, 2, 5, 10, 24, 48, 72 and 96 h. The concentrations of target compounds were determined by the pretreatment and analytical methods as described in 3.2.2.

Table 6.1 Batch experimental design on variation of SRT

	R1		R2		R3	
Removal routes[a]	A	B+A	A	B+A	A	B+A
SRT (d)	18		30		over 60	
MLSS (mg/L)	8,380		14,340		21,800	
MLVSS (mg/L)	6,680		11,450		17,000	
Standard (μg/L)	+[b]	+	+	+	+	+
NaN_3 (%, w/v)	+	-	+	-	+	-
Aeration (mg/L)	+	+	+	+	+	+

[a] B-biodegradation and A-adsorption

[b] + showed with or added, - showed without or not added.

6.2.1.2 Experiment on the effect of AOB and NOB

Batch experiments were performed to evaluate correlations between biodegradation of PPCPs and autotrophs, specifically AOB and NOB using four flasks with different conditions, as described in Table 6.2. In AOB experiment (e.g., A1 and A2), initial concentration of ammonia was controlled at approximately 20 mg-N/L concentration using ammonium chloride to make nitrifying conditions. Also, in NOB experiment (e.g., N1 and N2) approximately 5 mg-N/L and 20 mg-N/L of ammonia and nitrite were

injected as initial concentration using ammonium chloride and sodium nitrite, respectively to evaluate biodegradation of target compounds under nitrite oxidizing conditions. Since allylthiourea (ATU) has been employed as selective inhibitor of nitrification (Bedard et al., 1989; Ginestet et al., 1998), 30 mg/L of ATU was used to inhibit ammonia oxidation. Experiments were conducted using MBR sludge with the same MLSS concentration (8,380 mg/L) and standard solution and aeration were applied to each flask. Concentration of nitrite and nitrate were determined by analytical instrument, ion chromatography (Dionex, ICS-1000) and ammonia nitrogen was determined with the Nessler method approved by U.S.EPA in which the test was using by spectrophotometer DR 2000 (Hach., 1992).

Table 6.2 Batch experimental design on the effect of AOB and NOB

	AOB experiment		NOB experiment	
	A1	A2	N1	N2
S_{NH} (mg-N/L)	20	20	5	5
S_{NO2} (mg-N/L)	- [a]	-	20	20
MLSS (mg/L)		8,380		
MLVSS (mg/L)		6,680		
Standard (µg/L)	100	100	100	100
ATU (mg/L)	-	30	-	30
Aeration (mg/L)	+	+	+	+

[a] + showed with or added, - showed without or not added.

6.2.2 Description of ammonia oxidation

Nitrification is a two-step oxidation process of ammonium or ammonia to nitrate catalyzed by two ubiquitous bacterial groups (Ward., 1996; Morris et al., 2009) and the molecular mechanism is summarized in Figure 6.1. The first step is oxidation of ammonium to nitrite by AOB represented by the *nitrosomonas* species. Specifically, ammonia is initially oxidized to hydroxylamine by presence of oxygen and enzyme catalyzed by AMO. Hydroxylamine is then oxidized to nitrite by electrons and another enzyme catalyzed by hydroxylamine oxidoreductase (HAO). The second step is

oxidation of nitrite to nitrate by NOB represented by the *nitrobacter* species. Nitrite produced in the first reaction of autotrophic nitrification is oxidized to nitrate by nitrite oxidoreductase (NXR).

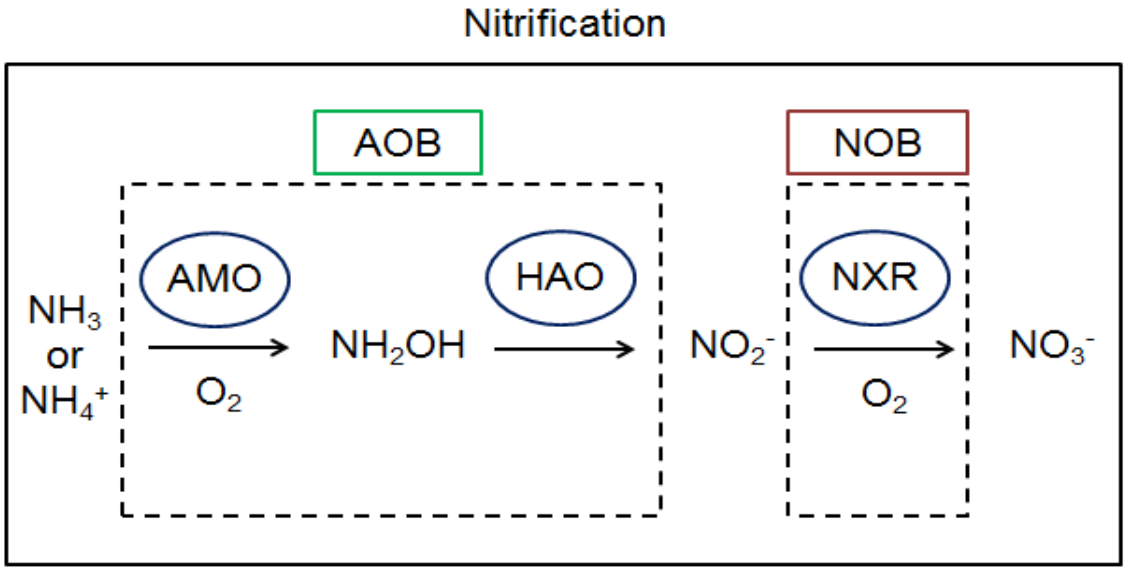


Figure 6.1 Schematic diagram of nitrification process by AOB and NOB

6.2.3 Measurement of cometabolic degradation

A Monod-type equation expressing the effect of substrate concentration on the growth of nitrifying bacteria has been found to fit the data in most nitrification studies (Barnes et al., 1983). As can be seen in Eq.2.3, modified kinetic models including various parameters such as temperature, oxygen concentration and pH have also been applied in wastewater treatment in accordance with each condition. In general, slow growing autotrophic bacteria use oxidation of ammonia as their sole source of energy. The growth rates of AOB are thus directly related to the availability of ammonia and the kinetics of its oxidation (Prosser., 1989).

In this work, ammonia oxidation rate ($q_{NH3\text{-}N}$, $mg_{NH3\text{-}N}/g_{VSS}\cdot d$) were determined by the produced rate of nitrite and nitrate per time for MLVSS concentration and cometabolic degradation rate (q_{PPCPs}, $\mu g_{PPCPs}/g_{VSS}\cdot d$) of each compound was expressed by attenuated concentration of PPCPs per time for MLVSS concentration during ammonia oxidation through linear regression analysis. Moreover, in order to evaluate the potential of cometabolic degradation, transformation yields (T_y), which are the mass of PPCPs degraded per unit mass of ammonia consumed, were estimated (Kocamemi et al., 2010).

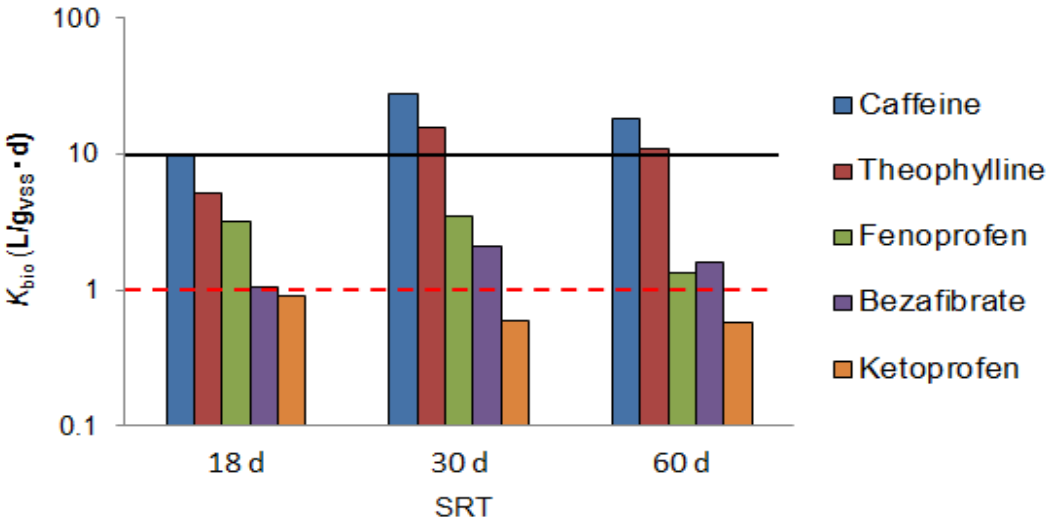
6.3 Results and discussion

6.3.1 Removal of PPCPs by variation of SRT

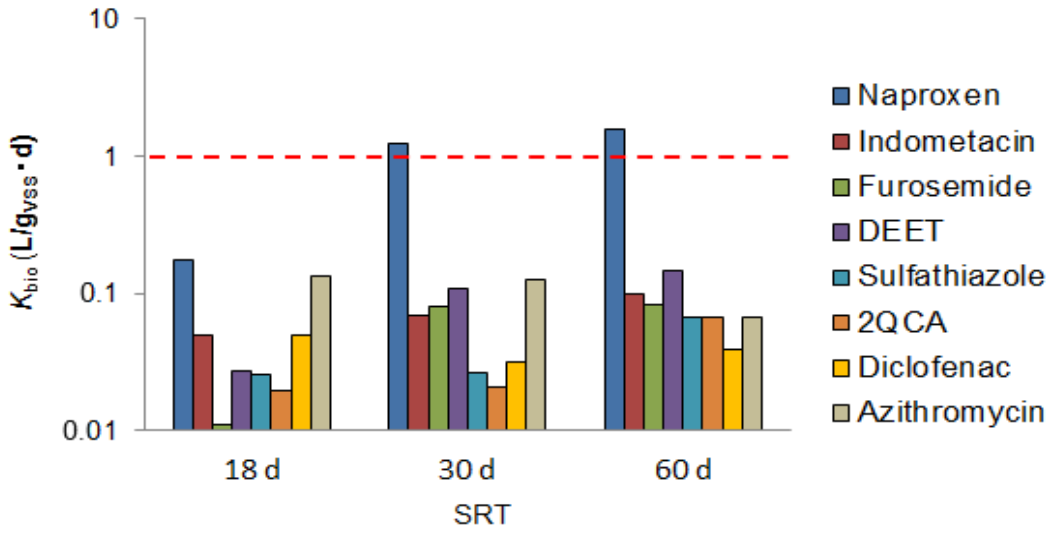
Biodegradability of MBR sludge with three different SRT (18, 30 and over 60 d) was investigated in terms of removal of PPCPs and the parameters including rate constants, half-lives, K_{bio} and K_d values are summarized in Table 6.3. From the results obtained in Chapter V, very highly biodegradable compounds found in MBR with above 10 L/g_{VSS}·d of K_{bio} values, such as caffeine and theophylline, showed significant removal efficiency regardless of variation of SRT, even though relatively lower K_{bio} values were observed at low SRT (18 d). Similar pattern was shown in the cases of fenoprofen and bezafibrate which were highly biodegraded in MBR. These substances were greatly eliminated at all studied SRT conditions, with half-lives ranging from 0.6 to 1.3 h in fenoprofen and from 0.9 to 2.7 h in bezafibrate. For ketoprofen, about two times higher K_{bio} value was noted at 18 d, but other parameters like first-order rate constant and half-lives were not significantly varied, which can be described by difference of relative concentration caused by higher MLVSS concentration developed at 30 and 60 d in comparison with 18 d. Taken together, above mentioned five compounds were independent on the variations of SRT and thus they can be efficiently removed in MBR process operating at least 18 d (Figure 6.2 (a)).

On the other hand, naproxen exhibited lower K_{bio} value (0.175 L/g_{VSS}·d) at 18 d, whereas biodegradability of naproxen increased to 1.563 L/g_{VSS}·d at above 60 d. Furthermore, as can be seen in Figure 6.2 (b) removal of some compounds showing higher biodegradation tendency in MBR than CAS, but were hardly degraded with lower K_{bio} values, such as indometacin, furosemide, DEET, sulfathiazole and 2QCA, found to be effective with increasing SRT. K_{bio} values of these substances increased from 0.050, 0.011, 0.027, 0.025 and 0.020 L/g_{VSS}·d at 18 d to 0.099, 0.084, 0.146, 0.067 and 0.066 L/g_{VSS}·d at 60 d in indometacin, furosemide, DEET, sulfathiazole and 2QCA, respectively. Although the biodegradability of these PPCPs was not much greater at condition of high SRT, it was apparent that change of MLSS concentration by increased SRT had impact on the removal of these compounds. That is, their persistent behavior observed in lower MLSS concentration can be partially improved with variation of MLSS concentration (i.e., the prolonged SRT), which also is able to explain the discrepancy of biodegradation capability between MBR and CAS biomass. As claimed by several studies, relatively high SRT in the MBR was capable of more efficient removal of antibiotics by enriching different bacteria types and bioaccumulation of more complex

organic molecules (Clara et al., 2004; Le-Minh et al., 2010). Although no enough data was found in literature to compare our results, some studies reported the removal efficiency of selected compounds in MBRs and CAS operating at different SRTs, in which naproxen and sulfathiazole showed better removal performance at long SRT (around 50 d) and slightly higher values was found at around 30 d regarding removal of diclofenac (Kosma et al., 2010; PILLS Report., 2012; Verlicchi et al., 2015).



(a) Compounds having high K_{bio} values



(b) Compound having low K_{bio} values

Figure 6.2 K_{bio} values of each compound as a function of variation of SRT

10 < K_{bio}: very highly biodegradable (black solid line), 1 < K_{bio}: highly biodegradable (red dotted line) and 0.1 > K_{bio}: hardly biodegradable.

Table 6.3 Summary of parameters obtained in batch experiments on variation of SRT

Compounds	SRT (d)	Rate constant (h^{-1})	Half-lives (h)	K_{bio} ($L/g_{VSS}\cdot d$)	R^2	K_d (after 10 h) (L/kg)
CAF	18	1.630	0.4	9.960	0.92	29.5
	30	5.513	0.1	27.979	1.00	13.2
	60	3.079	0.2	17.952	1.00	37.1
TEP	18	1.328	0.5	5.120	0.95	7.9
	30	6.049	0.1	15.394	1.00	10.2
	60	5.843	0.1	10.946	1.00	7.5
FP	18	0.786	0.9	3.207	0.98	18.5
	30	1.228	0.6	3.435	0.99	36.8
	60	0.549	1.3	1.339	0.91	35.0
BZF	18	0.257	2.7	1.036	0.85	16.5
	30	0.813	0.9	2.070	0.94	26.2
	60	0.797	0.9	1.585	0.99	24.3
NPX	18	0.045	15.5	0.175	0.93	15.0
	30	0.587	1.2	1.231	0.92	24.9
	60	0.773	0.9	1.563	0.96	21.9
KTP	18	0.222	3.1	0.909	0.95	15.0
	30	0.280	2.5	0.587	0.91	24.5
	60	0.285	2.4	0.570	0.95	22.4
MFA	18	0.009	79.6	0.050	0.95	59.9
	30	0.044	15.8	0.092	0.97	120.0
	60	0.024	29.0	0.034	0.98	240.1
IDM	18	0.014	49.9	0.050	0.92	30.2
	30	0.033	20.9	0.069	0.93	77.1
	60	0.070	9.9	0.099	0.95	78.8
FSM	18	0.008	88.7	0.011	0.96	19.2
	30	0.031	22.2	0.080	0.93	33.7
	60	0.042	16.5	0.084	0.92	32.2
DEET	18	0.004	158.6	0.027	0.95	20.9
	30	0.041	17.0	0.109	0.94	26.3
	60	0.068	10.1	0.146	0.97	23.2
2QCA	18	0.005	127.6	0.020	0.96	14.8
	30	0.010	69.5	0.021	0.99	18.2
	60	0.047	14.8	0.066	0.97	20.7

(Continued)

Compounds	SRT (d)	Rate constant (h^{-1})	Half-lives (h)	K_{bio} ($L/g_{VSS}\cdot d$)	R^2	K_d (after 10 h) (L/kg)
STZ	18	0.007	98.4	0.025	0.91	14.1
	30	0.013	54.4	0.027	0.99	26.5
	60	0.047	14.6	0.067	0.97	25.3
DCF	18	0.031	22.6	0.110	0.96	35.5
	30	0.022	31.3	0.046	0.90	66.3
	60	0.028	24.6	0.040	0.97	85.0
AZM	18	0.027	26.0	0.131	0.96	74.9
	30	0.030	23.1	0.125	0.95	59.1
	60	0.019	36.6	0.068	0.92	56.2

These results on fate of naproxen were consistent with higher biodegradability observed in our study, but some results were quite different from our results. For example, diclofenac and azithromycin showed the highest K_{bio} values at 18 d, with 0.110 and 0.131 $L/g_{VSS}\cdot d$, whereas these values decreased to 0.040 and 0.068 $L/g_{VSS}\cdot d$ when working at SRT above 60 d. It means that these compounds were not dependent on SRT in MBR operation, even though better biodegradation was achieved in MBR compared with CAS sludge.

To sum up, the study on whether biodegradation of target compounds can be strongly affected by variation of SRT in MBR process was investigated and further the following subdivision of compounds according to their biodegradability with different SRT is proposed:

- Highly biodegradable compounds (K_{bio} values > 1 $L/g_{VSS}\cdot d$) were not dependent on the variations of SRT, in which their biodegradation capability was not significantly changed by further increase of MLSS concentration.
  (e.g., caffeine, theophylline, fenoprofen, bezafibrate and ketoprofen (only moderately biodegradable))
- Hardly biodegradable compounds (K_{bio} values < 0.1 $L/g_{VSS}\cdot d$) were intimately related to SRT, in which enhanced biodegradability was obtained as SRT increased. Thus, these compounds are expected to be better eliminated by a prolonged SRT.
  (e.g., naproxen (only moderately biodegradable), indometacin, furosemide, DEET, sulfathiazole, and 2QCA)
- Another case of hardly biodegradable compounds showed different degree of

biodegradation regardless of the change of SRT. To better understand these compounds, it needs to study other important factors which are capable of controlling biodegradation, such as operating parameters and the nature of microbial population.
(e.g., mefenamic acid, diclofenac and azithromycin)

6.3.2 Inhibition of AOB activity

AOB experiments were subdivided into A1 (without AOB inhibition) and A2 (with AOB inhibition) using ATU, respectively. In order to identify biological oxidation of ammonia, the change of nitrite, nitrate and ammonia concentration over time with no AOB inhibition was observed and the results are represented in Figure 6.3, in which ammonia concentration decreased rapidly from 20.5 mg/L to 1.2 mg/L within 5 h, whereas nitrate concentration increased correspondingly from 0.7 mg/L to 20.4 mg/L. After 10 h, subsequent increase of nitrate and decrease of ammonia concentration was not obtained, in which the change of nitrite concentration was negligible. It means that ammonia was ultimately transformed to nitrate by nitrifiers like AOB which are able to use the ammonia as an energy source in the initial period of experiment.

Also, Figure 6.4 shows the variation of ammonia concentration over time with and without ATU addition. Unlike A1, there was no significant change of ammonia concentration in A2, indicating that the AOB activity in experiment using MBR sludge was definitely inhibited.

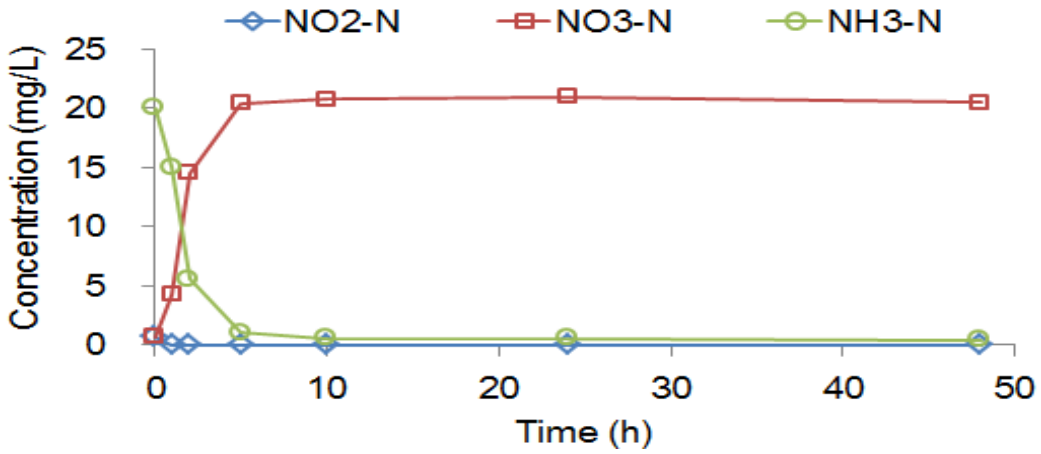


Figure 6.3 Profile of NO_2-N, NO_3-N and NH_3-N concentration with no AOB inhibition

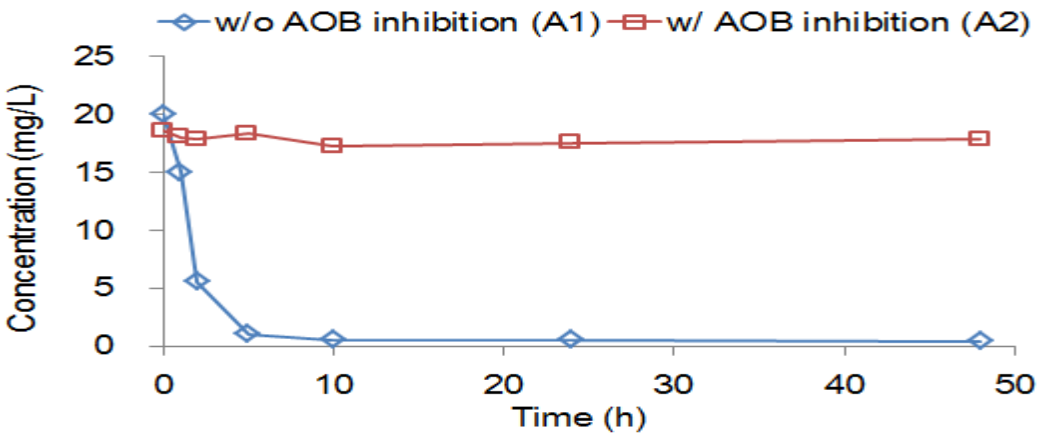


Figure 6.4 Profile of NH_3-N concentration with and without AOB inhibition

6.3.3 The role of AOB in removal of PPCPs

Batch tests were conducted to study the importance of nitrifying bacteria in MBR sludge in terms of biodegradation of PPCPs, and variations of observed concentrations of target compounds in A1 and A2 are shown in Figure 6.5. Also, estimated parameters are summarized in Table S-2 of SI. With respect to beta blockers, as shown in Figure 6.5 when ammonia oxidation was completed decrease of initial atenolol concentration was rapidly achieved within 5 h in both A1 and A2, but even higher K_{bio} value was observed in A1 (2.168 L/g_{VSS}·d) than in A2 (1.399 L/g_{VSS}·d), which was consistent with other results of batch experiment. According to Sathyamoorthy et al. (2013), they reported that biodegradation rate coefficient for atenolol was 2.39 ± 0.21 L/g_{VSS}·d under nitrification conditions and 0.56 ± 0.10 L/g_{VSS}·d under nitrification inhibition conditions. In another work, biodegradability using MBR biomass operating at 18 d SRT was represented as suspended solids normalized value and showed 0.98 L/g_{SS}·d (Maurer et al., 2007), which was similar to our results (1.115 L/g_{TSS}·d). Moreover, metoprolol was found to be completely eliminated when nitrification was not inhibited, while the removal was not rapidly obtained when oxidation of ammonia was limited. K_{bio} value of this substance showed 0.801 and 0.176 L/g_{VSS}·d, with 3.1 and 14.2 h of half-lives in A1 and A2, respectively, in which about 4-5 times higher biodegradation capability was revealed via nitrification. Wick et al. (2009) reported that 0.35 and 0.40 L/g_{SS}·d of metoprolol was biologically transformed by biomass taken from the aerated zone of the second activated sludge operated at 18 d SRT in unit of the WWTP Frankfurt, which was lower than K_{bio} values of A1 obtained from our study, but higher than K_{bio} values of A2. Other beta blockers, such as metoprolol and propranolol, or diltiazem also had smaller K_{bio} values in the absence of nitrification, suggesting that this group having a similar

chemical structure may be degraded by uniform pattern with enzymes that are engaged in biotransformation.

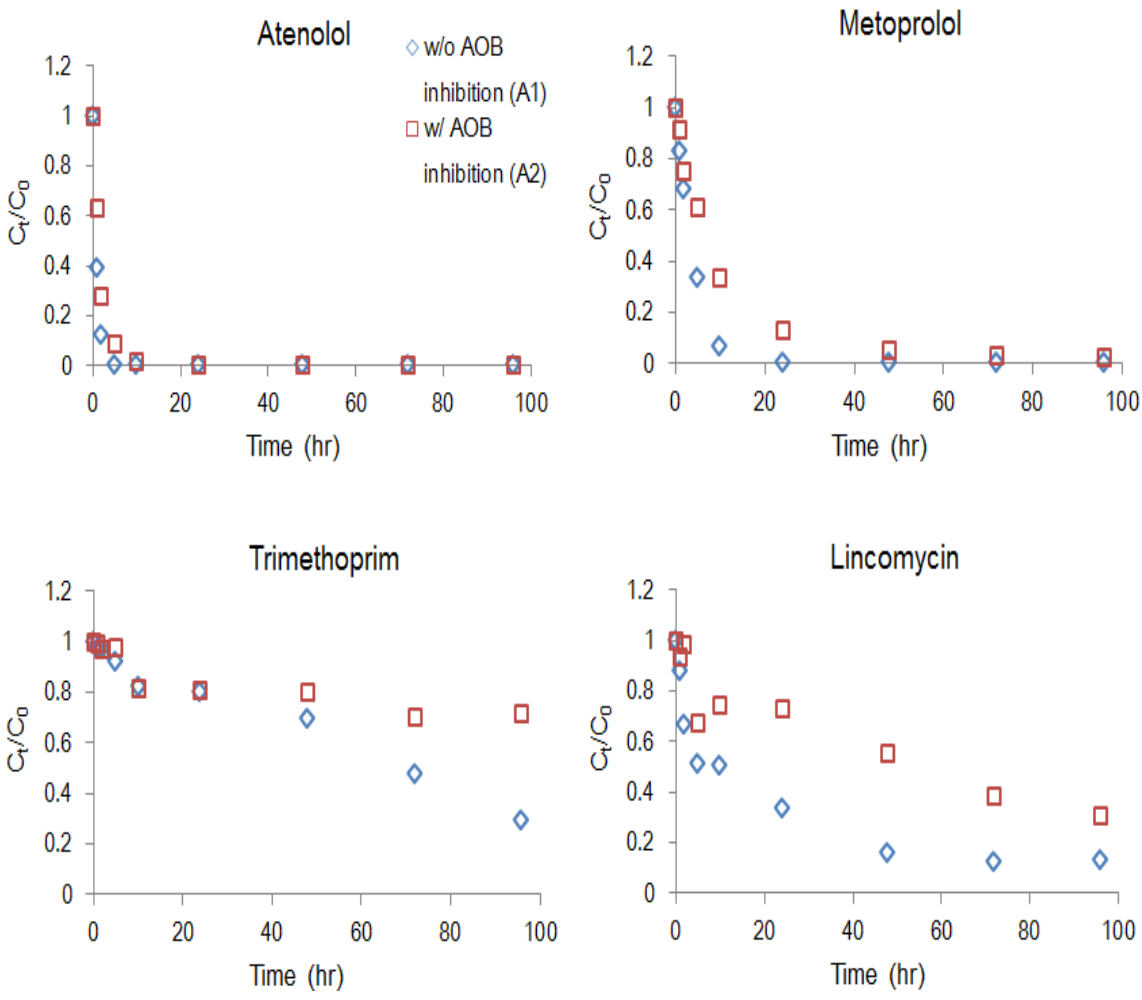
When the activity of AOB was not inhibited the removal of trimethoprim, is an antibiotic used widely for treating chest or urine infections, was 70%, whereas when nitrification was inhibited the removal reached to 28%. K_{bio} values normalized by MLVSS concentration for trimethoprim were 0.041 and 0.013 $L/g_{VSS}\cdot d$ in A1 and A2, with half-lives of 61.4 h and 198.1 h, which was in good agreement with previously reported study by Batt et al. (2006), who demonstrated degradation rate of 0.01 h^{-1} with no inhibition of nitrification and 0.002 h^{-1} with inhibition of nitrification. Similarly, for lincomycin, it has been known as recalcitrant antibiotic in biodegradation by WWTPs, with removal efficiency ranging from no significant removal to less than 50% (Karthikeyan et al., 2006; Carucci et al., 2006; Gao et al., 2012), 87% of initial concentration was attenuated after 96 h in A1, with K_{bio} value of 0.077 $L/g_{VSS}\cdot d$ and half-lives of 32.2 h, but relatively low removal (about 70%) was observed in A2, with K_{bio} value of 0.041 $L/g_{VSS}\cdot d$ and half-lives of 60.6 h. In comparison with A2, the biodegradability in A1 was approximately 3 times and 2times greater in trimethoprim and lincomycin, suggesting that AOB played a key role in the biodegradation of two compounds with MBR sludge. This is consistent with our assumption that some substances have been found to be greater removal in MBR compared with CAS can be efficiently eliminated in nitrification enrichment community.

Enhanced biodegradability was also clearly indicated in some contaminants like 2QCA and mefenamic acid. In A1, removal of 2QCA and mefenamic acid reached to 95% and 85%, while the removal remarkably decreased by 21% and 19%, respectively. The K_{bio} values obtained from A1 showed 0.069 and 0.072 $L/g_{VSS}\cdot d$ in 2QCA and mefenamic acid, but the values decreased to 0.009 and 0.010 $L/g_{VSS}\cdot d$ in A2. Furthermore, since adsorption tendency was lower (less than 100L/kg) and was not varied during sampling events, removal by adsorption was not considered. Compared with other compounds, there was a big difference of K_{bio} values between A1 and A2 (7 times higher values in A1), showing that attenuation of concentration was significantly inhibited by the absence of nitrifying bacteria. On the contrast, although naproxen and furosemide had smaller biodegradation rate in A2, initial concentration was found to be completely eliminated in naproxen and was considerably attenuated in furosemide at a slow rate, showing that rapid oxidation via nitrification was linked to removal of these compounds, but limited condition also allowed them to be degraded.

Moreover, although comparable or higher biodegradability was achieved under nitrification conditions, removal of readily biodegradable compounds such as caffeine,

theophylline, fenoprofen and ketoprofen was rapidly obtained in both cases, with half-lives ranging from 0.5 to 1.5 h in A1 and from 0.5 to 4.7 h in A2. It means that these substances were efficiently eliminated by microbial activity developed in MBR process, but their removal was not greatly affected by the presence of AOB.

In general, for biological processes including nitrogen treatment, the removal efficiency of PPCPs is greater than other systems like submerged biofilters or fixed biomass reactors (Miège et al., 2009; Hester et al., 2015). It can be also demonstrated by our results, in which remarkably increased K_{bio} values when AOB inhibition was not achieved provide clear evidence that nitrification by AOB has important impacts on the biodegradation of some target compounds. Unfortunately, however, it is very difficult to compare these parameters because the experiments on a link between biodegradation of PPCPs and nitrification were not conducted in other studies. Accordingly, there is no way to evaluate whether observed biodegradation was achieved by nitrifying bacteria or heterotrophic activity.



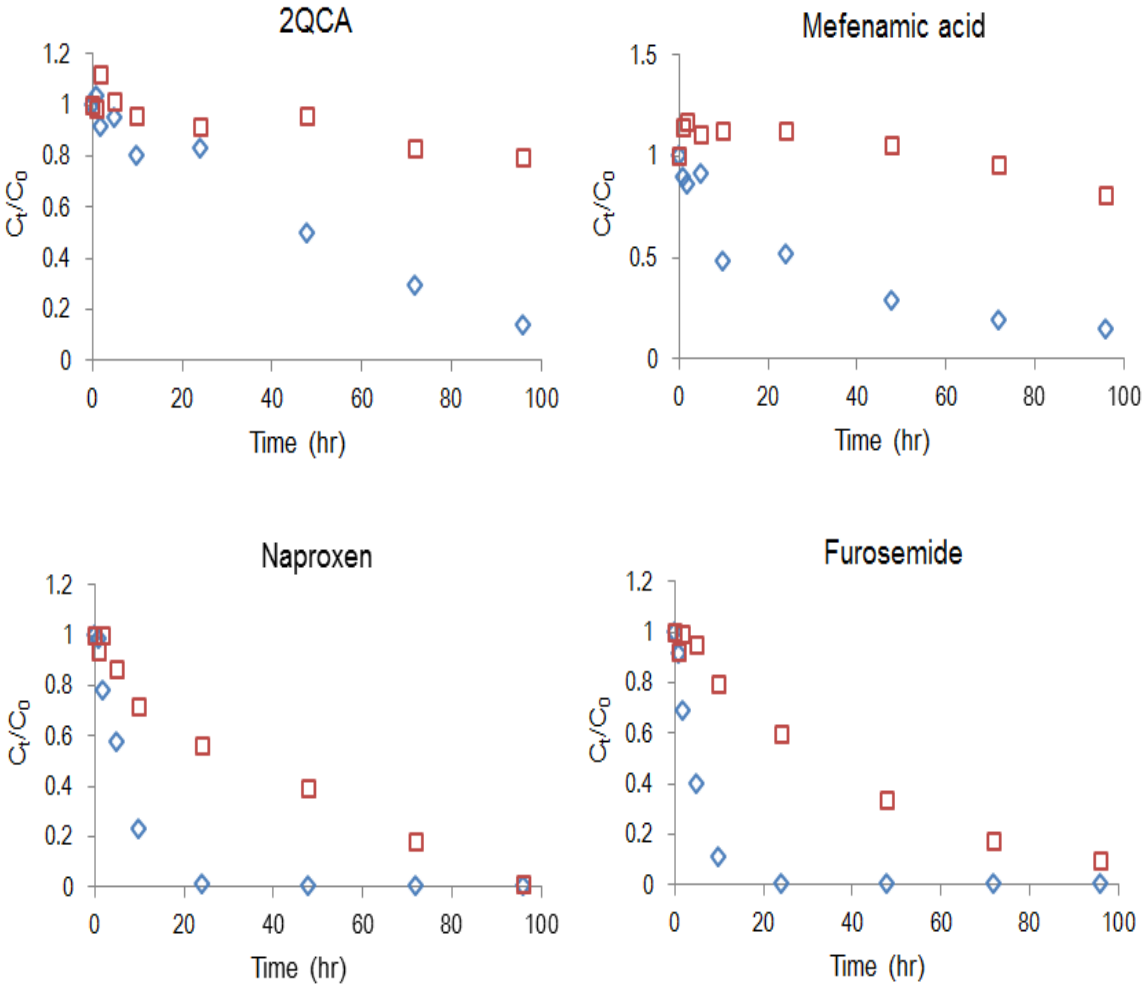


Figure 6.5 Changes of relative concentration of target compounds with and without AOB inhibition

6.3.4 Degradation rates of AOB, NOB and HET

NOB experiments were performed to assess the influence of nitrite oxidation on removal of PPCPs and herein addition of initial nitrite concentration had an intention of supplying nitrite produced in the first step of autotrophic nitrification. Figure 6.6 shows the change of nitrite, nitrate and ammonia concentration over time under nitrite oxidizing conditions, in which nitrite concentration decreased from 17.5 to 1.5 mg/L within 10 h and 90% of initial concentration was oxidized. While ammonia was completely eliminated during same experimental period, nitrate concentration correspondingly increased from 1.7 to 23.1 mg/L by conversion of ammonia and nitrite concentration, but further increase was not observed after 24 h. This result indicates that our experimental design was well established to identify biodegradation of target compounds under the

conditions of nitrite oxidation, but there is some probability that oxidation of AOB by small amounts ammonia might be involved in degradation of NOB, thereby leading to difficulties on distinguishing between influence of AOB and NOB.

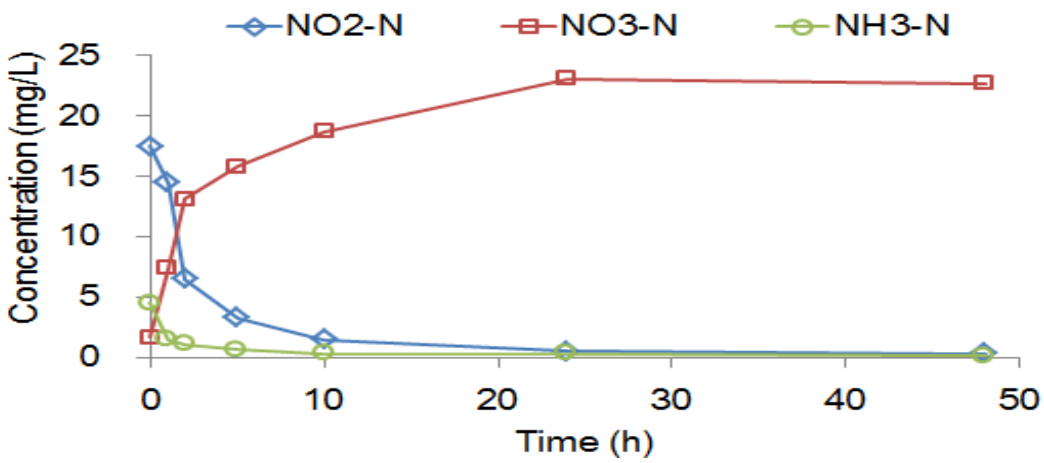


Figure 6.6 Profile of NO_2-N, NO_3-N and NH_3-N concentration under nitrite oxidizing conditions

Table 6.4 shows estimated degradation rates of AOB, NOB and HET, respectively, in which fraction degraded by each bacterial group is also included. Degradation rates of bezafibrate, fenoprofen, azithromycin and tylosin by HET varied in the range from 0.62 to 5.10 $\mu g_{PPCPs}/g_{VSS}\cdot d$ and were much higher than those by AOB and NOB, for which over 97% fraction was found in all compounds. Thus, it was concluded that these compounds were well degraded regardless of nitrification. Also, theophylline and caffeine showed higher degradation rates by HET, with fractions of 84.9 and 68.0%, even though attenuation of concentration was significantly achieved with oxidation of nitrifying bacteria. Diclofenac and DEET were not completely eliminated under all conditions, but removal by HET was greater than other bacteria, with fractions of 68.3 and 70.1%.

On the other hand, degradation rates of naproxen, furosemide, metoprolol and propranolol were 1.99, 2.13, 2.36 and 0.95 $\mu g_{PPCPs}/g_{VSS}\cdot d$, respectively, and found to be the highest in AOB, with fractions ranging from 51.8 to 71.5%, suggesting that they were greatly affected by energy obtained from oxidation of ammonia while conversion of ammonia to nitrate was performed. Higher degradation rates by AOB were also observed in diltiazem and mefenamic acid, including 62.1 and 69.1%. It is noteworthy considering that some compounds relevant to activity of AOB were almost completely eliminated before 24 h when nitrification was not inhibited. In other words, although AOB

and NOB can coexist in the enriched nitrification conditions and play a key role in degradation of PPCPs, influences of AOB was predominant over NOB in terms of removal of above mentioned substances. It can be clearly explained by the fact that the growth rate of AOB is faster than that of NOB. For instance, the growth of *nitrosomonas* ranged from 8 to 36 h, whereas the growth of *nitrobacter* ranged from 12 to 59 h. Bacterial growth rate that is typically expressed using specific growth rate was higher in AOB (0.33 to 2.2 d^{-1}) than NOB (0.14 to 1.39 d^{-1}) (Grady et al. 1999; AWWA. 2006). Inversely, sulfonamide antibiotics, such as sulfamethoxazole, sulfamerazine, sulfamonomethoxine, sulfapyridine and sulfadimethoxine, were highly degraded by NOB, with NOB fractions ranging from 59.6 to 83.0%. Unlike some compounds involved in degradation by AOB, sulfonamide antibiotics were continuously eliminated after oxidation of ammonia was completed, suggesting that some NOB clusters closely associated with degradation of these substances, thereby allowing them to be cometabolised or cooxidised via the transformation of nitrite to nitrate at slow rate.

6.3.5 The potential of cometabolic degradation

Some studies have suggested that a wide range of micro organic pollutants like PPCPs and EDCs can be oxidized by non-specific enzymes, AMO (Chang et al., 2003; Shi et al., 2004; Kim et al., 2011). Cometabolism of PPCPs is apparently noted in autotrophic bacteria such as AOB and NOB (Tran et al., 2013). Conversely, readily biodegradable compounds were not relevant to cometabolic degradation. For instance, Roh et al. (2009) reported that non-ammonia oxidizing microorganisms were likely to be responsible for readily biodegradable compound, like ibuprofen. In this work, therefore, based on results of A1 and A2 comparative study between cometabolic degradation during ammonia oxidation and biodegradation by non-ammonia oxidizing bacteria (i.e., heterotrophic bacteria) was investigated. Cometabolic degradation rates were calculated by subtracting A2 from A1 using mass balance, as seen in Figure 6.7 and Table 6.5. Atenolol of degradation rate showed 15.42 and 7.12 $\mu g_{PPCPs}/g_{VSS}\cdot d$ in A1 and A2, respectively, for which highest cometabolic degradation rate (8.30 $\mu g_{PPCPs}/g_{VSS}\cdot d$) was observed among selected target PPCPs, even though removal by heterotrophic bacteria was found to be highly eliminated. Effect of cometabolism on removal of atenolol was also suggested by Helbling et al. (2012). Their studies have shown a close relationship between stable removal efficiency of ammonia concentration and removal of atenolol, explaining that it was associated with biotransformation reactions by the abundance of ammonia oxidizing microorganisms.

Table 6.4 Estimated degradation rates of AOB, NOB and HET and their fraction

Target compounds	AOB		NOB		HET	
	D.R[a] $\mu g_{PPCPs}/g_{VSS}\cdot d$	Fraction %	D.R $\mu g_{PPCPs}/g_{VSS}\cdot d$	Fraction %	D.R $\mu g_{PPCPs}/g_{VSS}\cdot d$	Fraction %
Atenolol	7.15	46.4	1.15	7.5	7.12	46.2
Ketoprofen	5.13	49.4	1.01	9.7	4.24	40.9
Theophylline	4.68	12.5	0.98	2.6	31.81	84.9
Caffeine	3.48	25.2	0.94	6.8	9.40	68.0
Naproxen	1.99	51.8	0.90	23.4	0.95	24.8
Furosemide	2.13	57.2	0.60	16.2	0.99	26.6
Metoprolol	2.36	60.5	0.29	7.6	1.25	31.9
Propranolol	0.95	71.5	0.07	5.0	0.31	23.4
Sulfamethoxazole	0.09	8.1	0.86	73.1	0.22	18.8
2QCA	0.17	14.2	0.72	60.8	0.30	25.0
Diltiazem	0.83	62.1	0.01	0.8	0.50	37.1
Sulfamerazine	0.01	0.9	0.77	83.0	0.15	16.1
Sulfamonomethoxine	0.05	5.5	0.73	78.3	0.15	16.3
Sulfapyridine	0.03	4.1	0.55	65.9	0.25	30.0
Sulfadimethoxine	0.08	9.9	0.49	59.6	0.25	30.5
Indometacin	0.25	26.2	0.31	32.5	0.39	41.4
Antipyrine	0.36	57.0	0.18	28.9	0.09	14.1
Isopropylantipyrine	0.20	35.4	0.27	46.2	0.11	18.4
Mefenamic_acid	0.34	69.1	0.09	18.5	0.06	12.3
Clofibric_acid	0.04	5.9	0.38	64.6	0.17	29.5
Trimethoprim	0.31	46.0	0.08	11.9	0.29	42.1
Sulfathiazole	0.04	3.2	0.31	26.0	0.84	70.8
Lincomycin	0.24	25.8	0.10	11.2	0.59	62.9
Diclofenac	0.08	12.6	0.12	19.0	0.42	68.3
Crotamiton	0.06	19.9	0.11	36.4	0.13	43.7
DEET	0.09	18.8	0.05	11.1	0.34	70.1
Bezafibrate	0.07	2.2	0.01	0.3	3.29	97.6
Fenoprofen	0.03	0.6	0.00	0.0	5.10	99.4
Azithromycin	0.01	1.6	<0	<0	0.62	98.4
Tylosin	0.02	1.7	<0	<0	0.95	98.3

D.R[a]: Degradation rate and <0: not available value by incorrect mass balance.

With respect to readily biodegradable substances such as ketoprofen, theophylline and caffeine, significantly higher cometabolism was achieved, with cometabolic degradation rates ranging from 4.22 to 6.13 $\mu g_{PPCPs}/g_{VSS}$·d. On the other hand, no differences between degradation rate in the presence of AOB inhibition and in the absence of AOB inhibition were obtained in other highly degradable compounds like bezafibrate and fenoprofen, indicating that nitrification process were unlikely to be responsible for degradation of these compounds. Above mentioned four compounds such as atenolol, ketoprofen, theophylline and caffeine showed greatly higher rates in even A2, which means these substances can be easily removed in the conditions of ammonia oxidation as well as in the community composition of heterotrophic bacteria. Our results were partially consistent with available previous studies. According to Tran et al. (2013), who reported that heterotrophic microbe can involve in the both cometabolism and metabolism in accordance with the concentration of PPCPs and their toxicity to the microbial populations. In another work, ATU was only used as inhibitor of AMO activity in nitrifiers, in which despite of inactivation of nitrifying bacteria higher degradation in ibuprofen and partial degradation in ketoprofen were observed during degradation period probably due to the activity of heterotrophs. In addition to ibuprofen and ketoprofen, initial concentration of some NSAIDs such as naproxen, indometacin and diclofenac were found to be reduced by 35%, 30% and 20%, respectively in case of ATU addition (Tran et al., 2009). Cometabolic degradation rates of some compounds such as naproxen, furosemide and indometacin were 2.89, 2.73 and 0.56 $\mu g_{PPCPs}/g_{VSS}$· d, which exhibited 3-5 times higher rates in A1 in comparison to those obtained in A2. It indicates that removal of these compounds was achieved by not only adaption of heterotrophic bacteria, but also the effect of autotrophic ammonia oxidizers using enzymes involved in cometabolic degradation.

Moreover, with the exception of sulfathiazole five sulfonamide antibiotics such as sulfamethoxazole, sulfamerazine, sulfamonomethoxine, sulfapyridine, and sulfamethoxine were found to be efficiently eliminated by cometabolic degradation, with cometabolic degradation rates ranging from 0.57 to 0.95 $\mu g_{PPCPs}/g_{VSS}$ · d, while biodegradation of these substances was not greatly affected by heterotrophic bacteria. According to Müller et al. (2013), who suggested that biodegradation of sulfamethoxazole was observed with activated sludge after a lag phase of 14 d and bacteria capable of degrading sulfonamide antibiotics was usually presented in activated sludge consortia. Also, García-Galán et al. (2012) claimed that for sulfonamide antibiotics increase of removal efficiency might be caused by the long SRT often applied in MBR process which offers sufficient adaption for heterotrophic bacteria

to degrade persistent pollutants and growth of slow growers such as nitrifiers. However, from our studies these compounds were independent to variation of SRT in MBR conditions, and thus cometabolic degradation can be described by enhanced ability of nitrifying bacteria, particularly by NOB, to catalyze nonspecific oxidation rather than diversity of microbial community caused by the a prolonged SRT.

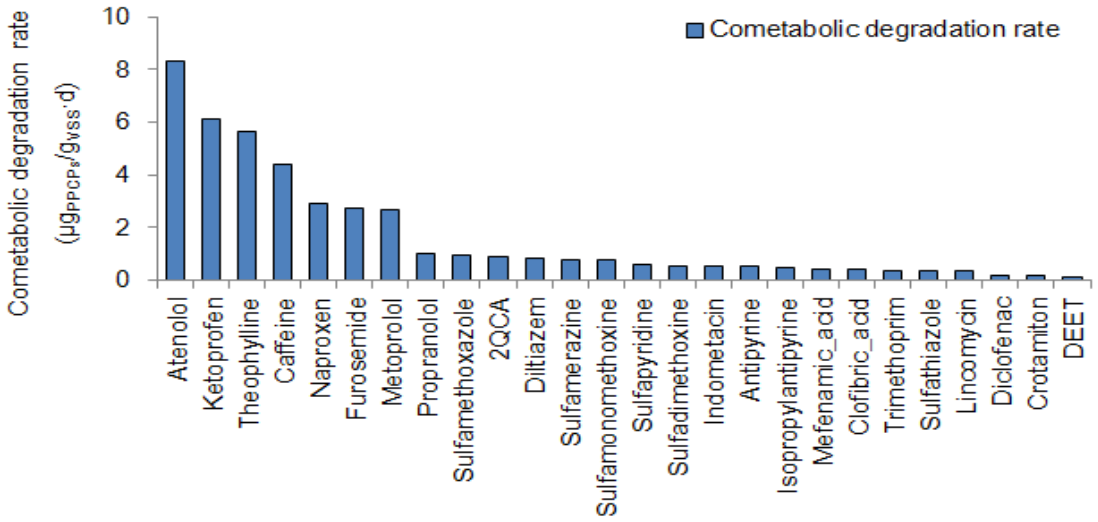


Figure 6.7 Cometabolic degradation rates of PPCPs

As can be shown in Table 6.5, T_y values of 30 out of 45 compounds were investigated to express potential of cometabolic degradation. Other 15 compounds were not available because the concentration was not attenuated during sampling period (i.e., no degradation) or incorrect mass balance was observed in some substances with high adsorption tendency. Ammonia oxidation rates were represented by MLVSS concentration and showed 6.35 and 0.01 $mg_{NH3\text{-}N}/g_{VSS}$·d in A1 and A2 experiments, respectively. T_y values of each compound ranged from 0.01 to 1.31 $\mu g_{PPCPs}/mg_{NH3\text{-}N}$ and minimum and maximum values were found in bezafibrate and atenolol, respectively. It is not surprising that these values were directly proportional to cometabolic degradation rates because identical ammonia oxidation rate was utilized.

Moreover, the minimum amount of ammonia concentration required for the degradation of 1 μg PPCPs was determined by using reciprocal of T_y values and these values also will be used as parameters for developing predictive model. Therefore, the lower its value is, the higher the amount of compounds being cometabolised at a given ammonia oxidation rate. Among target compounds, the lowest values were found as 0.77 mg NH_3-N in atenolol, followed 1.04 mg NH_3-N in ketoprofen, 1.12 mg NH_3-N in

theophylline, 1.44 mg NH_3-N in caffeine, 2.19 mg NH_3-N in naproxen, 2.33 mg NH_3-N in furosemide and 2.39 mg NH_3-N in metoprolol, while the highest values turned out to be 77.43 mg NH_3-N in bezafibrate, followed 43.42 mg NH_3-N in DEET, 37.06 mg NH_3-N in crotamiton, 32.63 mg NH_3-N in diclofenac. In particular, T_y values estimated from our study for some substances were quite comparable with those reported by Fernandez-Fontaina et al. (2014). They conducted the kinetic experiments on cometabolic biotransformation in nitrifying reactors, in which the transformation capacity was found to be 0.47, 0.08 and below 0 $\mu g_{PPCPs}/mg_{NH3\text{-}N}$ in naproxen, sulfamethoxazole and diclofenac, respectively. Also, although target compounds and experimental conditions like mixed cultures and initial concentration were different, other studies on cometabolic degradation of xenobiotic trichloroethylene (TCE) and chlorinated solvents showed 1.4 and 1.9 $\mu g_{TCE}/mg_{NH3\text{-}N}$, which were transformed by cometabolic degradation (Alvarez-Cohen et al., 2001; Kocamemi et al., 2010).

Table 6.5 Estimated cometabolic degradation rate and transformation yield

Target compounds	Cometabolic degradation rate (q_{PPCPs}) $\mu g_{PPCPs}/g_{VSS}\cdot d$	Transformation yield (T_y) $\mu g_{PPCPs}/mg_{NH3\text{-}N}$
Atenolol	8.30	1.31
Ketoprofen	6.13	0.97
Theophylline	5.66	0.89
Caffeine	4.42	0.70
Naproxen	2.89	0.46
Furosemide	2.73	0.43
Metoprolol	2.66	0.42
Propranolol	1.02	0.16
Sulfamethoxazole	0.95	0.15
2QCA	0.89	0.14
Diltiazem	0.84	0.13
Sulfamerazine	0.78	0.12
Sulfamonomethoxine	0.78	0.12
Sulfapyridine	0.58	0.09
Sulfadimethoxine	0.57	0.09
Indometacin	0.56	0.09
Antipyrine	0.54	0.08
Isopropylantipyrine	0.47	0.07

Mefenamic_acid	0.43	0.07
Clofibric_acid	0.42	0.07
Trimethoprim	0.39	0.06
Sulfathiazole	0.35	0.05
Lincomycin	0.34	0.05
Diclofenac	0.19	0.03
Crotamiton	0.17	0.03
DEET	0.15	0.02
Bezafibrate	0.08	0.01
Fenoprofen	0.03	0.00
Azithromycin	<0	<0
Tylosin	<0	<0

<0 indicates not available value by incorrect mass balance

6.4 Conclusions

Although it is widely known that long SRT, which is typically applied in MBR operation, can enhance the removal of a large variety of PPCPs by providing microbial community with enriched nitrifying cultures and various environmental conditions, there are still many unanswered questions. Therefore, in this work, elimination of PPCPs by variations of SRT was investigated and the distinct capability of nitrifying bacteria to degrade target compounds was also evaluated. From the estimated cometabolic and/or metabolic degradation rates, our study demonstrated why different removals were obtained in MBR process in terms of removal of PPCPs. Several conclusions can be drawn as follows:

1) Removal of highly biodegradable compounds was not dependent on the variations of SRT, whereas some moderate or hardly biodegradable compounds, such as naproxen, indometacin, furosemide and DEET were significantly affected by increase of SRT. It means that MBR process operating at the prolonged SRT can obviously provide conditions more conducive to biodegradation of some PPCPs.

2) Regarding removal of most compounds, initial concentration was rapidly attenuated with high K_{bio} values when activity of AOB was not inhibited, which provides clear evidence that nitrification by AOB which can cometabolize a wide array of PPCPs has

important impacts on the removal of PPCPs.

3) Both nitrifying and non-oxidizing bacteria were responsible for the degradation of PPCPs. Also, some compounds relevant to activity of AOB were relatively quickly eliminated, whereas in the case of sulfonamide antibiotics NOB was predominant over AOB while the rate of reaction steadily decreased after oxidation of ammonia was completed.

4) The estimated cometabolic degradation rates and transformation yields indicated the influences of nitrification rate on the degradation of PPCPs, in which compounds having greater values are able to be highly degraded by cometabolism derived from non-specific enzymes. Furthermore, these values were comparable to those reported by other studies and thus, they can be used as valuable parameters for predictive models.

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ChapterⅦ

Model-based Evaluation for Removal of PPCPs in MBR Process

7.1 Introduction

Modelling the fate of PPCPs in WWTPs is of present concern since it is very useful to enhance the removal performance of PPCPs and reduce their release to the environment (Pomiès et al., 2013). Predictive models also enable us to support regulatory rules and decisions. Even though there are no discharge requirements of PPCPs in the environment regarding the treatment of secondary effluent, Australian government has suggested some guidelines on limitation of PPCPs concentration in treated water for drinking water supplies. Few new PPCPs have been added to the list of priority substances, and as a result improved removal of PPCPs was observed in WWTPs (European Commission., 2012). In Switzerland, new plans on efficient management of emerging contaminants have been laid out for intensifying facilities of more than 100 WWTPs, with emphasizing enhanced removal of PPCPs. Also, the U.S. EPA has classified PPCPs as emerging pollutants and regulated the ordinance on the control of these compounds at state and municipal level (U.S.EPA, 2010). Like these examples, new directives and legal frameworks to protect and improve the quality of fresh water resources can be set up and renewed by development of practical models.

Moreover, there have been critical overviews of models proposed in the literature to illustrate removal of PPCPs in WWTPs with activated sludge process. For instance, Plósz et al. (2013) reported a comprehensive summary on modelling of PPCPs and transport in wastewater, in which current status were described and some recommendations were provided to improve and diffuse the use of such models with appropriate monitoring and detecting techniques. Also, Clouzot et al. (2013) discussed

that since a single model could not explain fate of various compounds, it was necessary for these tools to consider classes of PPCPs based on their chemical structure or ecotoxicological effect as well as removal mechanisms.

Some models have concentrated on the removal of PPCPs in MBR process, but it is very hard to predict exactly their fate and removal because elimination of substances was highly associated with not only internal factors like properties of PPCPs, but also external factors like operating conditions of WWTPs (Kovalova et al., 2012; Luo et al., 2014). Particularly, the tough thing is trying to correlate between various operating data and observed removal efficiency of PPCPs. In MBR, microbial activity is sensitive to operating conditions, and thus developing model to represent characteristics of biodegradation is a more complicated process. In addition, many PPCPs are biologically transformed by cometabolism, specific biochemical process of microorganisms to degrade non-growth substrates. Few studies have suggested that biotransformation rates have proved to be correlated to nitrification rate which is controlled by the concentration of autotrophic bacteria. They are known to catalyze non-specific oxidation of many organic xenobiotics such as PPCPs and EDCs (Batt et al., 2006; Wahman et al., 2006; Yi et al., 2007; Khunjar et al., 2011; Helbling et al., 2012; Fernandez-Fontaina et al., 2014). Also, these results were consistent with our findings. We have already studied that respective compounds can be eliminated by various mechanisms and enhanced conditions reported in MBR process, such as microbial diversity (e.g., effect by the prolonged SRT) and composition (e.g., nitrification by AOB activity), can be linked to their removal characteristics, thereby substantially improving the removal of target compounds. However, there is still insufficient information to understand effect of cometabolic degradation. Furthermore, input data like operating conditions and estimated parameters to see whether this provides applicability to enable reliable estimates to be made were not included in most papers.

Therefore, the overall objectives of this chapter were mainly divided into two parts; one is to predict the removal and fate of PPCPs considering the possible factors affecting removal of PPCPs with principal component analysis (PCA). Comparative study between simulated removal performance and those observed in pilot-scale MBR process was conducted. The other part is to apply cometabolic model based on ASM framework including the influence of microbial growth for removal of PPCPs with the experimental parameters and literature values. The model-based evaluation was also performed to validate the predictive model, with considering the influence and limitation of model parameters.

7.2 Materials and methods

7.2.1 Specification of pilot-scale MBR process

MBR operation was carried out on a pilot plant at WWTP located in K city, Japan. The water quality of influent and effluent is represented in Table 7.2. The raw wastewater was continuously fed into the anaerobic/anoxic/aerobic reactors after being sieved in a coarse screen. Ammonia sensor equipped in aerobic tank enabled to control the aeration rate with ammonia concentration of reactor, and thus reducing energy consumption of blowers in MBR. Also, two internal recycles to achieve efficient nitrogen removal and stabilization of settled sludge in aerobic tank were conducted from anoxic to anaerobic tank, and from aerobic to anoxic tank, respectively. The MBR compartment was equipped with MF hollow fiber modules in a submerged configuration and specification of pilot-scale MBR including membrane and operating conditions are shown in Table 7.1. To restrict membrane fouling, NaOCl was periodically used as chemical backwashing agent. Moreover, sampling events were conducted at twice a month during 16 months and target compounds were analyzed after pretreatment by methods represented in chapter 3.2.2.

Table 7.1 Operational specification of pilot-scale MBR

Parameters	Specification
Membrane type	Microfiltration (MF)
Module type	Hollow fiber
Membrane material	Polyvinylidene fluoride (PVDF)
Pore size	0.1 μm
Surface area	25 m^2 x 12
Temperature (℃)	21.8 (13.0 - 29.7)
pH	6.5 (6.0 - 7.6)
DO (mg/L)	5.7 (2.9 - 8.5)
MLSS (mg/L)	7,819 (5,040 - 10,600)
MLVSS (mg/L)	6,381 (3,920 - 7,880)

Table 7.2 Water quality of pilot-scale MBR process

Water quality	Influent	Effluent
BOD_5 (mg/L)	147.2 (±28.5)	0.7 (±0.5)
COD_{cr} (mg/L)	236.5 (±90.2)	9.4 (±4.6)
TSS (mg/L)	167.5 (±51.4)	ND
NH_3-N (mg/L)	16.3 (±6.0)	ND
TN (mg/L)	30.1 (±5.3)	8.7 (±5.3)
TP (mg/L)	3.5 (±0.8)	0.9 (±0.6)

ND stands for not detected and standard deviation of concentration are given in brackets.

7.2.2 Statistical analysis

7.2.2.1 Principal component analysis

Principal component analysis is a procedure for reducing a large set of variables in data to a smaller number of uncorrelated variables called principal components (Jolliffe., 2002; Ringnér., 2010). The goal of PCA is to explain the maximum amount of variance with the fewest number of principal components. It is widely used as a tool in exploratory data analysis and for making predictive models. Recently, this tool has been also applied in the field of wastewater treatment to conduct effective assessment on the occurrence and removal of PPCPs. For instance, Park et al. (2014) studied the occurrence characteristics of PPCPs and EDCs in lake water by developing the patterns between compounds in the cluster. The variance of target compounds were classified by mathematical method with PCA since overall removal efficiencies of PPCPs can be affected by different treatment types, seasonal effects and the nature of compounds (Guerra et al., 2014). According to Musolff et al. (2010), correlation and principal component analysis revealed a pronounced pattern of PPCPs in the urban water environments, in which seasonal attenuation is assumed to be a major process influencing the concentration of PPCPs.

Too much data including operating condition parameters and fate of target compounds can give rise to complexity in interpreting their relationships. Consequently, PCA was carried out to investigate the possible factors influencing the removal of PPCPs by reducing the number of dimensions and avoiding multicollinearity using IBM SPSS Statistics 21 and R for statistical calculations.

7.2.2.2 Model validation

Model validation by means of the Nash-Sutcliffe efficiency (NSE) coefficient was applied. Scientific researchers are commonly used to predict emerging contaminants in rivers and hydrological watershed (Moriasi et al., 2007; Aldekoa et al., 2016). It was a useful method to evaluate the correlations between modelled data based on estimated parameters by batch experiments and observed removal performance obtained from pilot-scale MBR process. The NSE is calculated as follows: (Nash et al., 1970)

$$\mathrm{NSE} = 1 - \frac{\sum_{i=1}^{n}\left(X_{obs,i} - X_{model,i}\right)^2}{\sum_{i=1}^{n}\left(X_{obs,i} - \overline{X_{obs}}\right)^2} \qquad \text{(Eq.7.1)}$$

Where, n is the total number of samples, X_{obs} and X_{model} are observed values and modelled values at time *i*, respectively, and $\overline{X_{obs}}$ is mean observed values. The resulting values range from -∞ up to 1.0. Essentially, the closer the model efficiency is to 1, the more accurate the model is. Strong predictive capability is generally characterized by NSE > 0.7 (McCuen et al., 2006).

As shown in Eq.7.2, the root mean square error (RMSE), which also called the root mean square deviation, RMSD, is a widely used for measurement of difference between values predicted by a model and the values actually observed. It shows good measure accuracy, but only to compare forecasting errors of different models for a particular variable and not between variables (Hyndman et al., 2006). In general, the lower this RMSE value is, the better the model is in its predictions.

$$\mathrm{RMSE} = \sqrt{\frac{\sum_{i=1}^{n}\left(X_{obs,i} - X_{model,i}\right)^2}{n}} \qquad \text{(Eq.7.2)}$$

Here, n is the total number of samples, X_{obs} and X_{model} are observed values and modelled values at time *i*, respectively.

7.2.3 Modeling equations and calculations

7.2.3.1 Predictive model based on biodegradation and adsorption

Eq.7.3 was used to predict removal fate and efficiency of target compounds, with operating data and experimentally estimated parameters, for which contribution of biodegradation, adsorption to sludge and discharge (no removal) were predicted, respectively and compared to mass balance calculated by Eq.3.1 in pilot-scale MBR.

$$\mathrm{C_{in}Q_{in}} = (K_{\mathrm{bio}}\mathrm{C_{in}XV}) + \left(\frac{\mathrm{XV}K_{\mathrm{d}}\mathrm{C_r}}{\mathrm{SRT}}\right) + (\mathrm{C_{out}Q_{out}}) \qquad \text{(Eq.7.3)}$$

Where, C_{in}, C_r and C_{out} are the concentration of PPCPs in influent, bioreactor and effluent, respectively (ng/L), Q_{in} and Q_{out} are the flow rates in influent and effluent, respectively (m^3/d), X is MLSS concentration (mg/L), V is volume of reactors (m^3), K_{bio} and K_d are estimated biodegradation constant rate (L/g_{MLSS}/d) and sludge-water distribution coefficient (L/kg), and SRT is solids retention time of MBR (d).

7.2.3.2 Predictive model based on cometabolic degradation

For nitrification kinetics, oxygen is a limiting factor controlling the growth of nitrifying bacteria in WWTPs. Moreover, more complex equations expressing the growth kinetics of nitrifying bacteria take into account the substrate concentration as well as environmental factors such as temperature, pH and DO concentration. Modified equation considering the effect of these parameters can be described as follows (Barnes et al., 1983):

$$\mu = \mu_{\mathrm{m}}\left(\frac{\mathrm{NH_3}}{\mathrm{K_N}+\mathrm{NH_3}}\right)\left(\frac{\mathrm{DO}}{\mathrm{K_{DO}}+\mathrm{DO}}\right)(\mathrm{C_{pH}}) \qquad \text{(Eq.7.4)}$$

Here, μ is the specific growth rate (d^{-1}), μ_m is the maximum specific growth rate (d^{-1}), K_N is the half saturation constant for ammonia substrate (mg/L), K_{DO} is the half saturation concentration for DO (mg/L), NH_3 is ammonia concentration (mg/L), DO is dissolved oxygen concentration (mg/L), and C_{pH} is pH constant. Also, the values of μ_m, K_N, and C_{pH} have been determined experimentally and represented by following equations (Eq.7.5, 7.6, and 7.7), respectively (Mandt et al., 1982; Sincero et al., 2003; Wang et al., 2009).

$$\mathrm{K_N} = 10^{0.051T-1.158} \quad \text{(Eq.7.5)}$$

$$\mu_{\mathrm{m}} = 0.47e^{0.098(T-15)} \quad \text{(Eq.7.6)}$$

$$C_{\mathrm{pH}} = 1 - 0.833(7.2 - \mathrm{pH}) \quad \text{(Eq.7.7)}$$

As mentioned in Chapter 2.5, the kinetic model to represent characteristics of biodegradation is described by pseudo first-order kinetics. Although this approach is considerably simple, it cannot figure out the effect of microbial composition and specific process occurring in bioreactor such as ammonia oxidation in terms of biodegradation of PPCPs. Hence, cometabolic process-based concept including Monod-type expressions for the growth and non-growth substrates was developed (Criddle., 1993). It was further integrated into ASM framework representing the microbial growth and utilization of substrate with nitrification process according to Sathyamoorthy et al. (2013), who suggested that three removal routes were found to be involved in biodegradation of PPCPs: 1) cometabolic biodegradation linked to AOB growth; 2) biodegradation by AOB in the absence of growth; and 3) biodegradation due to HET present in the bioreactor. As can be seen in Eq.7.8, the cometabolic model is used in this study to evaluate the contribution of cometabolic degradation and predict overall biodegradation of target compounds in MBR process with the experimental parameters and literature values.

$$\frac{\mathrm{dC}}{\mathrm{d}t} = -\{(T_{\mathrm{AOB}}\mu_{\mathrm{AOB}} + K_{\mathrm{bio-AOB}})\mathrm{X_{AOB}} + K_{\mathrm{bio-HET}}\mathrm{X_{HET}}\}\mathrm{C}$$

(Eq.7.8)

Where, C is the concentration of PPCPs (μg/L), T_{AOB} is the cometabolic transformation rate of PPCPs during ammonia oxidation (L/g), μ_{AOB} is the specific growth rate (d^{-1}), $K_{bio\text{-}AOB}$ is the normalized biodegradation rate without ammonia oxidation ($L/g_{VSS}\cdot d$), X_{AOB} is the AOB concentration (mg/L), $K_{bio\text{-}HET}$ is the normalized biodegradation rate by heterotrophic bacteria ($L/g_{VSS}\cdot d$) and X_{HET} is the HET concentration (mg/L).

7.2.4 Model parameters for cometabolic degradation

Model parameters used in this study are represented in Table 7.3. Specific growth

rate, μ value was determined from the μ_m and K_N which were calculated by suggested equations and operational conditions such as temperature, pH, DO level and ammonia concentration used in batch experiments. Furthermore, calculated and measured values were compared with the range of previous researches to confirm the validity of parameters in our study. Some parameters like X_{AOB} and X_{HET} were not measurable experimentally, so the values were selected with reference to the range of other studies, in which quantitative real-time PCR (qRT-PCR) was performed to estimate the total bacterial community. Various primer sets such as ammonia monooxygenase gene subunit (amoA-1F and amoA-2R) for AOB were used for determining the abundance of each composition. The *Nitrobacter* spp. and the *Nitrospira* spp. were measured using FGPS872, FGPS1269, NSR1113F and NSR 1264R, respectively (Dionisi et al., 2002; Wittebolle et al., 2008; Zhang et al., 2009; Sathyamoorthy et al., 2013).

Table 7.3 Model parameters used in predictive model on cometabolic degradation

Description	Notation	Unit	Range of values	References	Selected value
Maximum specific growth rate	μ_m	d^{-1}	0.45-1.40	3,6,7,9	*Cal.* 1.03
Half saturation constant for ammonia	K_N	mg/L	0.2-1	1,2,3	*Cal.* 1.0
Half saturation constant for oxygen	K_{DO}	mg/L	0.18-1.25	4,5,6	0.5
Conversion yield	Y_A	gCOD/gN	0.11-0.25	6,7,10,11	0.15
AOB	X_{AOB}	%	54-85	12,13	75
HET	X_{HET}	%	< 25	13	25
DO concentration	DO	mg/L	-	measured	4.0
Ammonia concentration	NH_3-N	mg/L	-	measured	20
Temperature	*T*	℃	-	measured	23
pH	pH		-	measured	6.7

Measured: Measured values and *Cal.*: Calculated values by equations.

References: 1. Vanrolleghem et al. (1999), 2. Van Haandel et al. (2007), 3. Sperandio et al. (2005), 4. Manser et al. (2005), 5. Sarioglu et al. (2009), 6. Henze et al. (1987), 7. Munz et al. (2011), 8. Jimenez et al. (2008), 9. Grady et al. (1999), 10. Jiang et al. (2005), 11. Sin et al. (2008), 12. Zhang et al. (2009) and 13. Sathyamoorthy et al. (2013).

7.3 Results and discussion

7.3.1 Factors affecting removal of PPCPs

Operating conditions are routinely varied to fulfill the water quality requirements for treating conventional pollutants and these parameters are expected to impact removal of PPCPs as well. For example, according to available literatures some conditions in WWTPs such as HRT, SRT, redox conditions and temperature were considered as important parameters (Eslamian., 2016). Alvarino et al. (2014) discussed the influence of main technological parameters in different biological treatment processes, for which removal routes as well as the effect of the operational conditions were necessary data to understand the removal efficiencies of PPCPs.

First of all, PCA was conducted to understand operating parameters related to biodegradation of PPCPs using data set accumulated during 16 months in pilot-scale MBR operation. Pilot-scale MBR was operated at stable condition with no significant variances of pH, redox condition of each compartment and inflow rate. In other words, HRT was fixed during operating period and contact time of the compounds within the reactor was not taken into account. Effect of membrane fouling represented by TMP was also not considered because backwashing by means of physical and chemical agents was periodically performed. On the other hand, some conditions, such as temperature, MLSS concentration, level of DO concentration are related to the activity and growth of microorganisms in MBR process. In addition, activity of nitrifying bacteria which are responsible for nitrification varies significantly with operational conditions and the extent of nitrification can be assumed by residual ammonia and nitrate concentration remaining in the effluent. The change of these conditions was consistently monitored throughout MBR operation and thus, the effect of operating parameters on removal performance of PPCPs (mainly biodegradation) could be studied.

For qualitative PCA, the first and second principal components accounted for 31% and 27% of total variance, respectively, for which about 60% of the variances contained in the data were retained by the first two principal components. As can be seen in Figure 7.1, all data points were projected into new coordinate system represented by two principal components to develop cluster map, in which each cluster was grouped and they were characterized by above mentioned four parameters (e.g., temperature, MLSS concentration, DO concentration and NO_3-N concentration in effluent). In other words, PCA classified the variance of target compounds into three groups depending on operating conditions. The characteristics and specific ranges of each cluster are

summarized in Table 7.4 and Table 7.5, respectively. As shown in Table 7.4, among three clusters group 1 was characterized by high temperature, middle NO_3-N and DO concentration, and low MLSS concentration. In group 1, ketoprofen, trimethoprim and diltiazem were grouped together with statistical significance (P values less than 0.05), which means that their removals were positively correlated to increase of temperature. It is interesting to note that among studied compounds 16 compounds with statistical significance were extracted and were expressed again on the factor map based on confidence interval at 95% for PCA components to reduce negative effect of noise on PCA, which making certain the accuracy of analysis (right side in Figure 7.2).

PPCPs which were involved in cluster 1 were negatively correlated with some substances involved in cluster 2 like azithromycin, clarithromycin, naproxen, furosemide and DEET which were positioned on opposite sides of the plot origin. Distribution of target compounds shows the relationships between all variables. The compounds belonged to cluster 2 were positively correlated to the MLSS concentration. In particular, in batch tests biodegradability of furosemide, naproxen and DEET were strongly dependent to MLSS concentration by change of SRT. In other words, PCA results can be used to support our findings on batch biodegradation experiments. Moreover, indometacin were included in group 3 which indicated high MLSS concentration and low temperature or NO_3-N concentration. In general, however, the longer the arrow, the more highly related that variable is to species composition. Thus, short length of arrow in DO and NO_3-N concentration suggested that they were less important factors in biodegradation of PPCPs compared with temperature and MLSS concentration.

To be short, although influent characteristics (e.g., initial concentration of PPCPs) and the extent of treatment achieved in process based on basic water quality parameters were not considered, PCA showed promising results on correlations between operating parameters and removal of PPCPs. Biodegradation was highly associated with temperature (e.g., ketoprofen, trimethoprim, diltiazem and diclofenac) and MLSS concentration (e.g., furosemide, naproxen, DEET, azithromycin and clarithromycin), but not significantly with DO level in reactors and residual NO_3-N concentration in effluent. For more understanding, further study by batch experiments is needed to investigate how temperature can affect biodegradation rate of PPCPs.

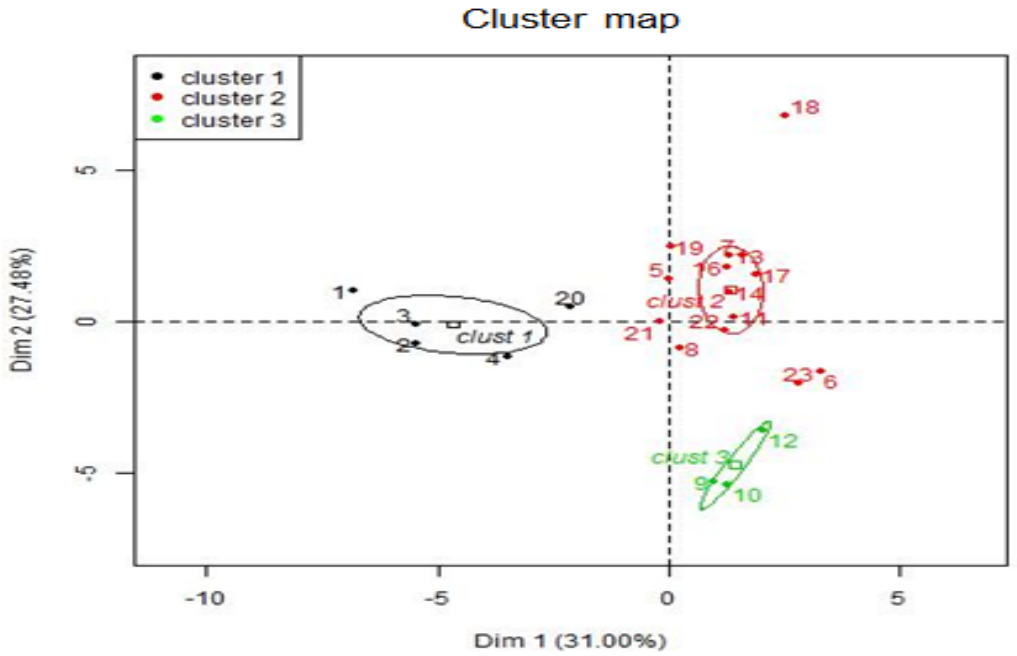


Figure 7.1 Cluster map for qualitative variables (target compounds)

Table 7.4 Characteristics of each cluster

Cluster	Temperature	MLSS concentration	NO_3-N conc. in effluent	DO level
1	H	L	M	M
2	M	H	M	M
3	L	H	L	H

H: high, M: medium, and L: low.

Table 7.5 Specific range of each cluster

Range	Temperature (℃)	MLSS concentration (mg/L)	NO_3-N conc. in effluent (mg/L)	DO level (mg/L)
High	27.3 (±0.7)	9568.8 (±194.9)	14.1 (±1.7)	6.8 (±0.3)
Medium	22.4 (±1.2)	7559.2 (±313.8)	9.2 (±1.2)	5.4 (±0.3)
Low	16.3 (±1.6)	6359.2 (±587.9)	4.8 (±0.8)	4.1 (±0.4)

Specific range is calculated by average value and standard deviation are given in brackets

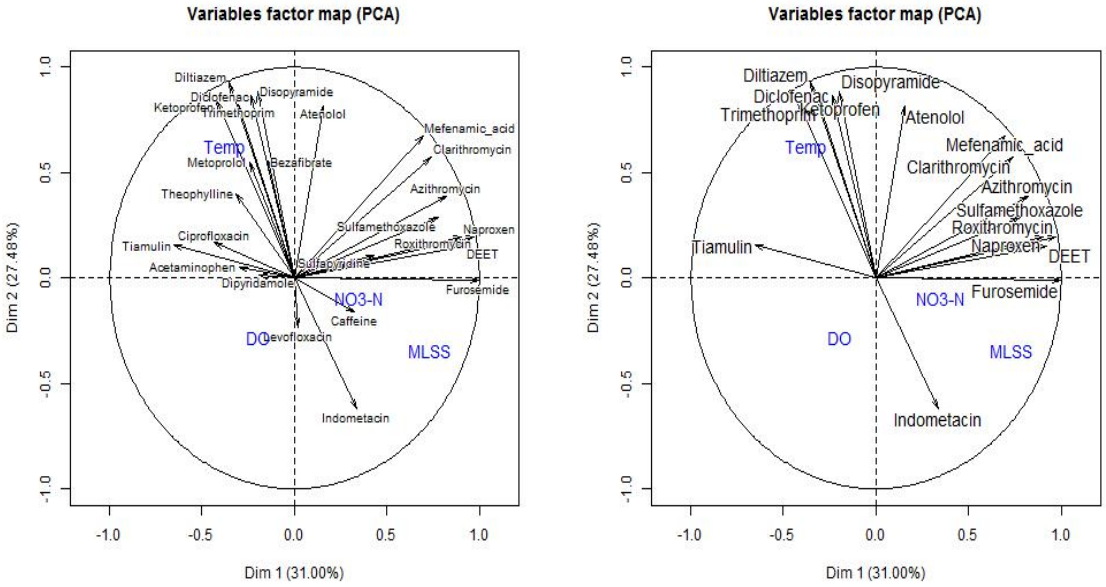


Figure 7.2 Factor map for all compounds (left) and 16 selected compounds (right) in principal component analysis

7.3.2 Prediction of removal performance

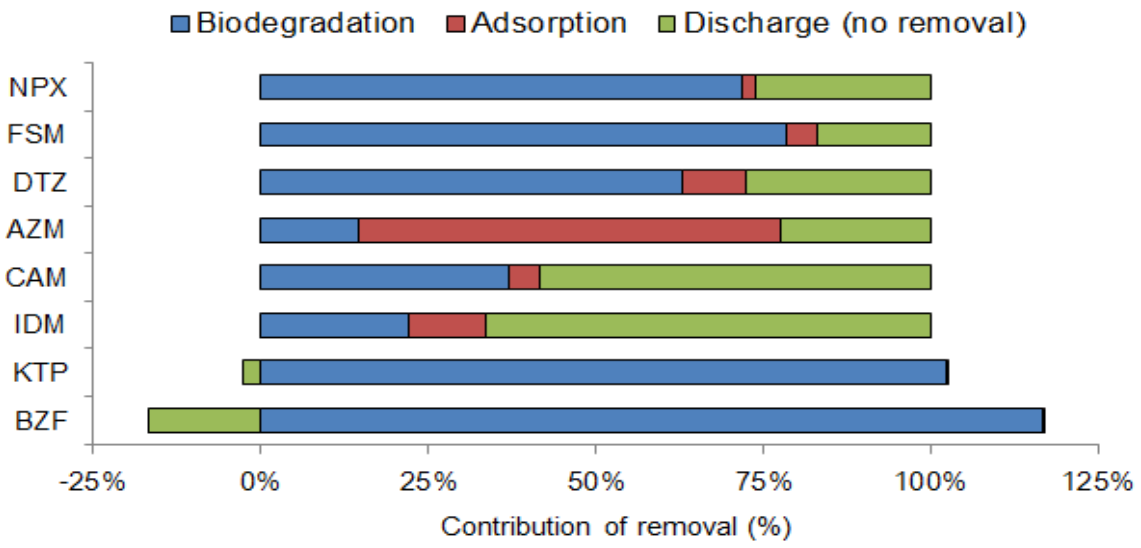
From the results of batch experiments and PCA, the possible factors affecting removal of PPCPs including biodegradation constant rate and adsorption affinity as well as the effect of operating conditions were reflected in equations of predictive model. In order to better clarify predicted and observed removal, a few considerations were sufficiently taken into account with respect to selection of target compounds. Firstly, in the aspect of observed removal, PPCPs which were detected at concentration level above 100 ng/L in influent of pilot-scale MBR process were only regarded as targets to exclude a sharp fluctuation in removal efficiency caused by low concentration of raw wastewater. Secondly, some compounds with high adsorption affinity (e.g., ciprofloxacin and levofloxacin) and readily biodegradable compounds (e.g., caffeine and theophylline) were not considered from the prediction because their mass balance was incorrect to describe the fate and contribution of removal. Lastly, the compounds which were dependent to the conditions of microbial activity were chosen to demonstrate correlations between operating parameters and removal characteristics of substances. As a consequence, eight compounds such as bezafibrate, ketoprofen, indometacin, clarithromycin, azithromycin, diltiazem, furosemide and naproxen were selected as target compounds and their removals were predicted by operating condition parameters

and estimated biodegradation and adsorption constants. Figure 7.3 and Table S-3 show contributions of removal via three routes such as biodegradation, adsorption and discharge (no removal) during MBR process.

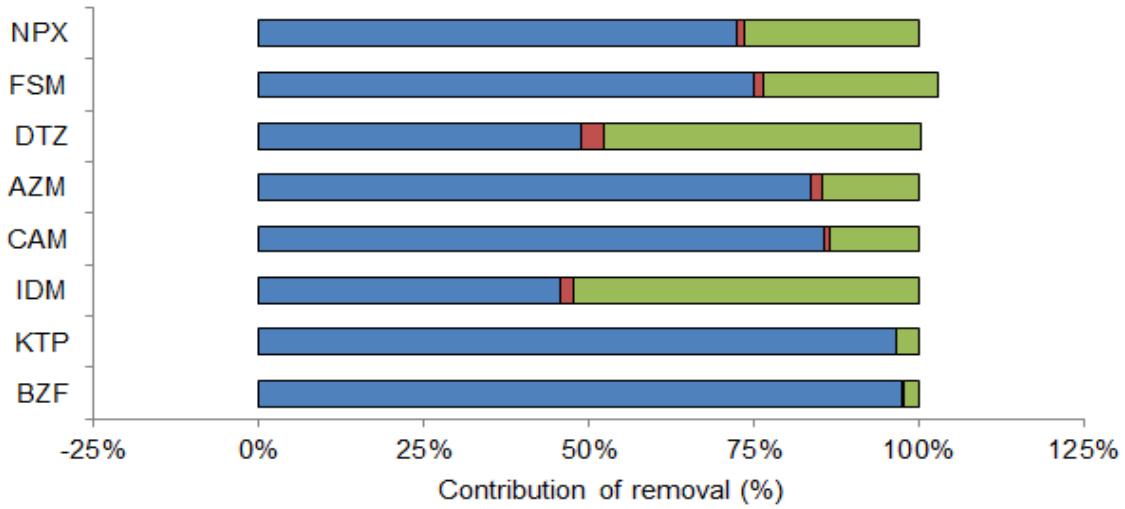
Although removal efficiency exceeding 100% was found in predicted biodegradation of bezafibrate and ketoprofen, as can be seen in Table 7.6 NSE coefficients were to be larger than 0.9 and approaching 1, suggesting that output of model for biodegradation was significantly associated with observed data. Like bezafibrate and ketoprofen, some compounds with higher biodegradability were rapidly degraded in biological treatment within a few hours, which resulted in inaccurate calculations of overall performance with removal efficiencies in the excess of 100%. Thus, it was concluded that removal performance of these compounds showing higher K_{bio} values than bezafibrate (1.036 $L/g_{VSS}\cdot d$) and ketoprofen (0.909 $L/g_{VSS}\cdot d$) was not able to be predictable. On the other hand, for furosemide and naproxen they exhibited significantly similar biodegradation between predicted and observed efficiency with above 0.98 in NSE values. For example, predicted biodegradation performance was 79% and 72% in furosemide and naproxen, while measured efficiency was 75% and 73%, respectively. Regarding above mentioned four compounds adsorption to sludge was considered as minor contributions and they showed higher biodegradability in accordance with conditions of microorganisms in reactors. Also, given that perfect match of predictive model was obtained, our model can be practically applied in MBR process to predict elimination of compounds which have these removal characteristics during treatment process.

In the case of indometacin and diltiazem, modelled removal efficiency for adsorption was to be slightly larger than observed mass balance, but this model seemed to be quite successful for simulating biodegradation with 0.73 and 0.86 of NSE coefficient. Specifically, predicted biodegradation showed 22% in indometacin and 63% in diltiazem, whereas 46% in indometacin and 49% in diltiazem were biologically degraded in pilot-scale MBR process. In contrast, biodegradability of azithromycin was predicted to be only 15%, while it was efficiently eliminated and removal efficiency reached to 84% in measured data which was partially consistent with our previous study on mass balance in lab-scale MBR process (72% removal in biodegradation). The significant differences between simulated and measured performance can be also described by NSE coefficient (0.25), in which the low values for biodegradation of azithromycin suggested limited predictive capability. Moreover, in comparison with other selected compounds, significantly higher adsorption capability was found to be in modelled adsorption removal of azithromycin based on K_d values and operating conditions like SRT, with 63% of removal efficiency, while measured removal efficiency was found to be only 2%,

which was in good agreement with previous results in lab-scale MBR (4%) and field study (1%). It was said that although SRT was included in model equations, not only excess sludge produced in pilot-scale MBR process was low, but also a big difference was obtained in K_d values between batch experiment and pilot-scale MBR, thereby causing substantially large efficiency in predictive removal performance. Therefore, it was concluded that this model seems to be more appropriate to predict removal efficiency of PPCPs which were not highly adsorptive but biodegradable.



(a) Predicted removal efficiency



(b) Observed removal efficiency

Figure 7.3 Contribution of (a) predicted and (b) observed removal in MBR process

Table 7.6 NSE coefficient for predicted and observed biodegradation

	BZF	KTP	IDM	CAM	AZM	DTZ	FSM	NPX
NSE coefficient (NSE)	0.96	0.97	0.73	0.64	0.25	0.86	0.99	0.98
Total number of samples (n)	22	22	17	21	22	21	16	16

7.3.3 Model-based evaluation for cometabolic degradation

Although biodegradation of PPCPs in biological treatment processes is usually predicted by the pseudo first-order kinetics, the role of microbial community composition in bioreactors and the effect of nitrification caused by AOB growth are not taken into account. However, predictive model proposed in Eq.7.8 included specific growth rate of microorganisms in accordance with environmental conditions and cometabolic biotransformation. The contribution of both biodegradation and adsorption capability in batch experiments were also considered, thereby ensuring more accurate prediction of fate and removal of target compounds. In order to obtain further insight into model performance, predictive model was compared to outputs by the pseudo first-order kinetics, in which the difference between modelled removal and observed values were evaluated.

Similar to prediction of removal performance using Eq.7.3, some aspects were considered important in cometabolic model. Firstly, the Key parameters of model contained T_{AOB}, μ_{AOB}, $K_{bio\text{-}AOB}$ and $K_{bio\text{-}HET}$, describing the cometabolic transformation, growth rate of AOB, biodegradation rate of AOB and HET, respectively and they were successfully determined by AOB and NOB experiments of Chapter VI (Table 7.7). Moreover, regarding target compounds observed reaction of some compounds such as caffeine, theophylline and fenoprofen reached equilibrium at less than 5 h. That is, they were almost completely eliminated in a very short time, which made it difficult to evaluate performance of two different models. For high adsorptive compounds, not only accumulated PPCPs concentration of biomass developed in MBR process was very high, but also the adsorption behavior of compounds onto MBR sludge was rapidly achieved. Consequently, incorrect mass balance was observed and comparative evaluation of these substances was not taken into consideration.

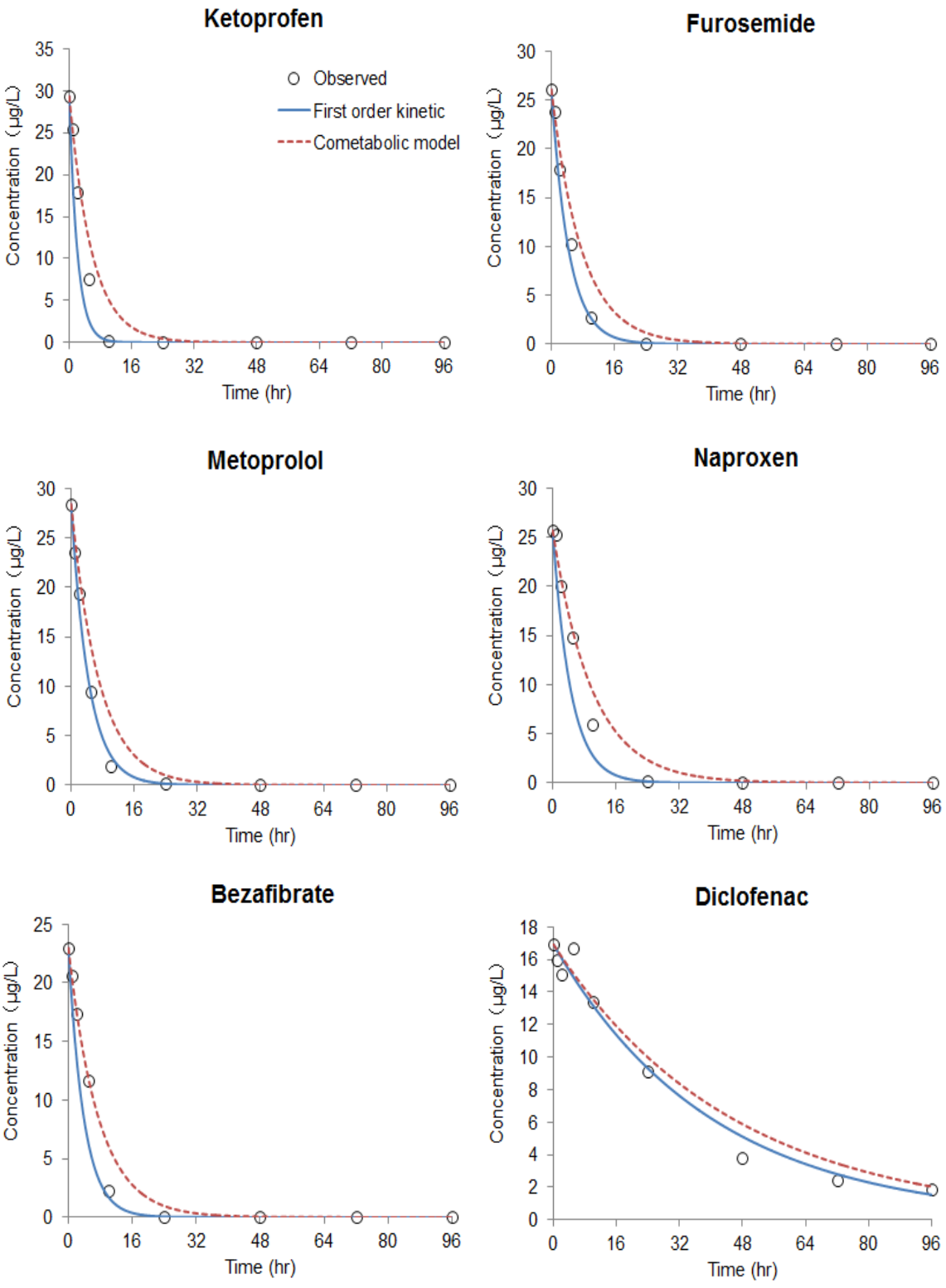


Figure 7.4 Comparison between observed and predicted removal for the compounds showing a high goodness of fit in pseudo first-order model

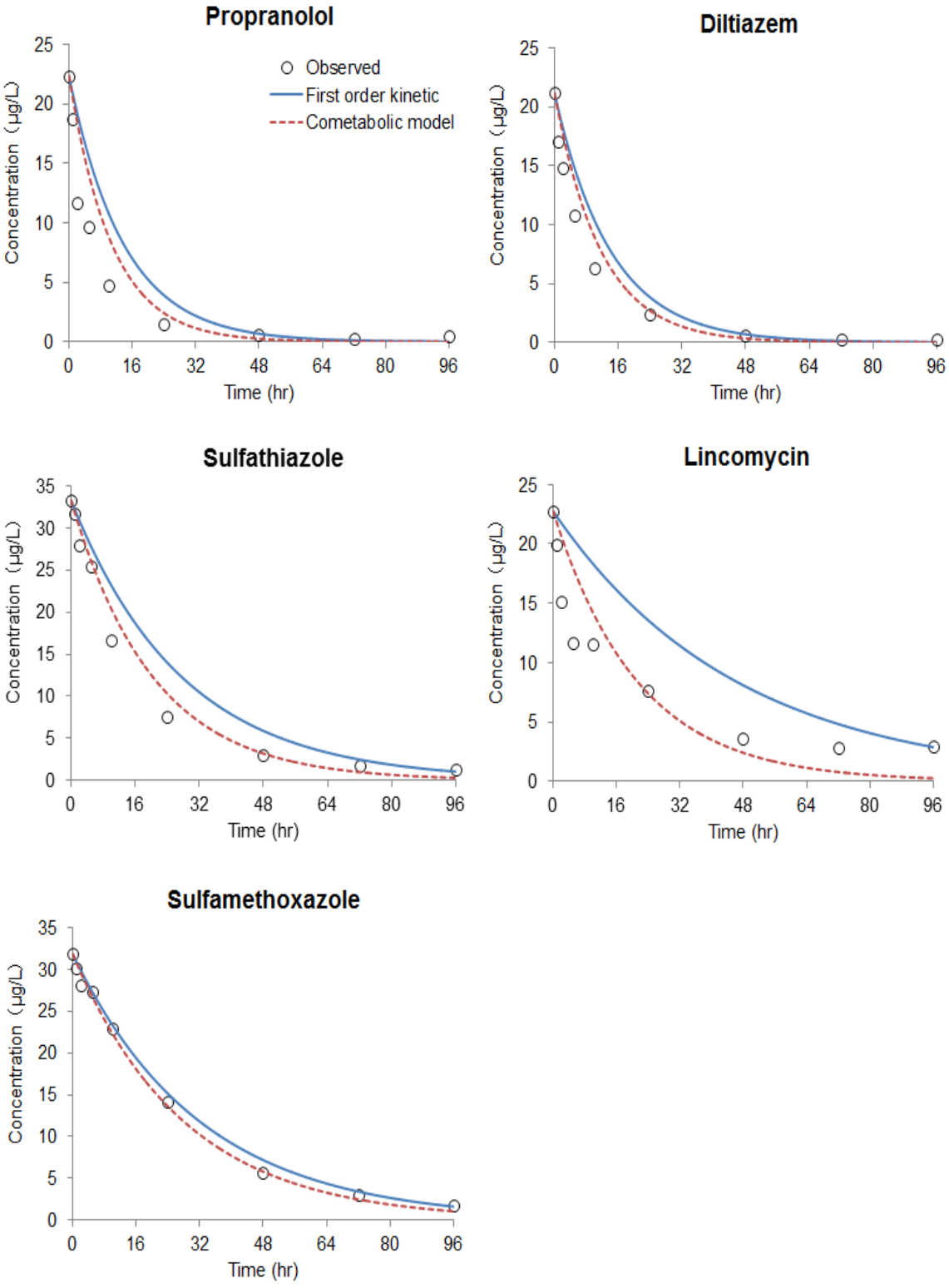


Figure 7.5 Comparison between observed and predicted removal for the compounds showing a high goodness of fit in cometabolic model

Table 7.7 Estimated model parameters for cometabolic model

Compounds	Cometabolic model		
	T_{AOB} L/g_{vss}	$K_{bio\text{-}AOB}$ $L/g_{VSS}\cdot d$	$K_{bio\text{-}HET}$ $L/g_{VSS}\cdot d$
Ketoprofen	1.01	0.12	0.53
Furosemide	0.69	0.23	0.09
Metoprolol	0.80	0.19	0.18
Naproxen	0.42	0.21	0.15
Bezafibrate	0.20	0.18	0.56
Diclofenac	0.01	0.09	0.04
Propranolol	0.60	0.12	0.02
Diltiazem	0.46	0.15	0.05
Sulfathiazole	0.19	0.12	0.04
Lincomycin	0.48	0.06	0.04
Sulfamethoxazole	0.11	0.11	0.01

Table 7.8 Goodness of fit for the cometabolic and pseudo first-order models

Compounds	Cometabolic model			Pseudo first-order model		
	R^2	RMSE	NSE	R^2	RMSE	NSE
Ketoprofen	0.96	5.95	0.94	0.98	3.42	0.98
Furosemide	0.97	4.78	0.96	0.99	0.22	0.99
Metoprolol	0.96	6.25	0.94	0.99	1.71	0.99
Naproxen	0.98	3.08	0.99	0.98	3.95	0.98
Bezafibrate	0.95	5.14	0.95	0.98	2.36	0.99
Diclofenac	0.98	1.82	0.99	0.98	0.73	0.99
Propranolol	0.91	6.66	0.90	0.88	8.72	0.82
Diltiazem	0.97	4.44	0.96	0.95	5.95	0.93
Sulfathiazole	0.98	3.56	0.99	0.96	8.13	0.97
Lincomycin	0.92	0.59	0.99	0.83	12.77	0.81
Sulfamethoxazole	0.99	0.53	0.99	0.99	2.61	0.99

Predicted removal of the cometabolic and pseudo first-order model as well as observed removal in batch experiments is represented in Figure 7.4, where target compounds showing a high goodness of fit in the pseudo first-order kinetics were drawn. To identify whether the model is an appropriate representation of PPCPs removal in MBR process, model accuracy was evaluated using R-squared, RMSE, and NSE values (Table 7.8). It was found to be larger cometabolic degradation rates in ketoprofen (6.13 $\mu g_{PPCPs}/g_{VSS}\cdot d$), naproxen (2.89 $\mu g_{PPCPs}/g_{VSS}\cdot d$), furosemide (2.73 $\mu g_{PPCPs}/g_{VSS}\cdot d$), and metoprolol (2.66 $\mu g_{PPCPs}/g_{VSS}\cdot d$), respectively. Results on the estimated model parameters for T_{AOB} and $K_{bio\text{-}AOB}$ also showed higher values compared with other substances, demonstrating that removal of these PPCPs was affected by either cometabolic transformation or biodegradation by autotrophic microbes. Even though cometabolic degradation was responsible for removal of these substances, the pseudo first-order model for removal of ketoprofen, furosemide and metoprolol except for naproxen was more accurate compared with predictive model on cometabolic degradation from the results of higher R-squared, NSE values and lower RMSE values. It can be explained by the results of batch experiments that these compounds showed high biodegradability with K_{bio} values ranging from 0.785 to 1.713 $L/g_{VSS}\cdot d$ and half-lives ranging from 1.5 to 3.1 h in MBR. As can be seen in Figure 7.4, they were completely eliminated in less than 24 h, indicating that parameters of cometabolic model, such as contribution of AOB and HET as well as the growth of AOB, were not adequately reflected in rapid reaction (i.e., fast biodegradation) and thus, removal of these compounds can be simply described by biodegradation constant represented by the pseudo first-order kinetics rather than the effect of cometabolic degradation.

Moreover, in the pseudo first-order model, a high proportion of the variability was achieved for bezafibrate (R^2: 0.98, RMSE: 2.36 and NSE: 0.99) and diclofenac (R^2: 0.98, RMSE: 0.73, and NSE: 0.99), whereas lower R-squared, NSE values and higher RMSE values were obtained in cometabolic model. Although a significant difference between accuracy of two models was not observed, removal of bezafibrate and diclofenac followed the pseudo first-order model. According to our results, heterotrophic bacteria were significantly involved in the removal of two compounds with very low cometabolic degradation rates (0.08 $\mu g_{PPCPs}/g_{VSS}\cdot d$ for bezafibrate and 0.19 $\mu g_{PPCPs}/g_{VSS}\cdot d$ for diclofenac, respectively), suggesting that their removal is not likely to be affected by degradation via cometabolic reactions.

On the other hand, it indicated that concentrations of propranolol, diltiazem and sulfathiazole were not completely attenuated at less than 24 h, and particularly, breakdown reactions were continuously sustained until the end of sampling events with

regard to the removal of lincomycin and sulfamethoxazole. It is not surprising that these compounds were rarely eliminated due to the insignificant adsorption affinity and moderate biodegradability (only poor removal for lincomycin) in MBR, with 0.260, 0.256, 0.130, 0.111 and 0.077 L/g_{VSS} · d in propranolol, diltiazem, sulfathiazole, sulfamethoxazole and lincomycin, respectively. Furthermore, it was found to be smaller degradation rate in HET, with $K_{bio\text{-}HET}$ values ranging from 0.1 to 0.5 L/g_{VSS}·d, while relatively higher rates were obtained in T_{AOB} and $K_{bio\text{-}AOB.}$ The degradation rates ranged from 0.11 to 0.60 in T_{AOB} and from 0.06 to 0.15 in $K_{bio\text{-}AOB}$, respectively.

In the aspect of model validation, the cometabolic model fitted observed removal data very well (Figure 7.5), in which three coefficients for evaluating correlations referred the closeness of measured value to predicted removal. The reasons for more precise results observed in the cometabolic model were suggested to be due to influence of cometabolic degradation related to AOB growth and biodegradation which was derived from AOB in the absence of growth. Unfortunately, since this model was only targeted for removal of atenolol in previous study comparative evaluation between our results and other studies was not conducted. For the above mentioned compounds, such as propranolol, diltiazem, sulfathiazole, sulfamethoxazole and lincomycin, the cometabolic model proposed in this study can help to describe the effect of biodegradation including cometabolic degradation in predicting the removal of PPCPs.

To sum up, following can be suggested to enable effective application of two different models:

- For ketoprofen, furosemide and metoprolol, although cometabolic degradation was significantly achieved, these substances in MBR were better described by the pseudo first-order model due to having a high biodegradability.
- In case of bezafibrate and diclofenac, since they were not greatly degraded by cometabolism, a high goodness of fit was obtained in the pseudo first-order model which was not capable of predicting the effect of nitrification as well as the growth of nitrifying bacteria.
- For the PPCPs showing moderate and poor biodegradability (e.g., propranolol, diltiazem, sulfathiazole, sulfamethoxazole and lincomycin), cometabolic model appeared to be an adequate fit to the observed data, in which the elimination was attributed to not only increased cometabolic degradation in MBR, but also little or no effect of heterotrophic bacteria.
- Given that PPCPs were modelled by different characteristics and divergent trend was observed in the removal of substances having the same therapeutic group and

similar chemical properties, the patterns of removal performance caused by both cometabolic degradation and biodegradation may substantially vary according to individual compounds.

7.3.4 Influence and limitation of model parameters on cometabolic degradation

In addition to experimentally estimated parameters such as T_{AOB}, $K_{bio\text{-}AOB}$ and $K_{bio\text{-}HET}$, the key component to cometabolic model was μ_{AOB}, which was represented by specific growth rate of AOB. Although μ_{AOB} was calculated by using the values from available literatures, the value may be changed quite substantially due to a broad range of reference values and experimental conditions applied in the batch study. Diversity and fractions of microbial populations like X_{AOB} and X_{HET} can make this model harder to predict removal of target substances. It is, therefore, important to note here that for the PPCPs with a high goodness of fit in cometabolic model, the sensitivity analysis was conducted based on the estimated values to identify the limiting factors in model approach and the potential of cometabolic degradation rate. Figure 7.6 illustrates analysis results of cometabolic degradation rate for target compounds depending on the variations of μ_{AOB} and fractions of X_{AOB}, in which identical parameters summarized in Table 7.3 except for μ_{AOB} in Figure 7.6 (a) and total number of AOB and HET in Figure 7.6 (b) were applied.

When the value of μ_{AOB} increased without changing fractions of AOB (75%), cometabolic degradation rates at μ_{AOB} of 1 d^{-1} were found to be improved by 80, 94, 66, 97 and 96% for sulfathiazole, lincomycin, sulfamethoxazole, propranolol and diltiazem, respectively. This tendency was clearly exhibited in lincomycin and propranolol, for which greater T_{AOB} values were observed compared with $K_{bio\text{-}AOB}$ and $K_{bio\text{-}HET}$, thereby causing the higher increase of cometabolic degradation. It means that cometabolic degradation rate was highly sensitive to the growth of AOB during ammonia oxidation. Moreover, as specific growth rate was constant as 0.5 d^{-1}, the decrease in the fractions of AOB affected the cometabolic degradation rate significantly. The performance increased from 24, 24, 5, 15 and 28% in 10% of AOB to 73, 84, 63, 92 and 91% in 90% of AOB, respectively. The number of AOB was considerably related to the both parameters of T_{AOB} and $K_{bio\text{-}AOB}$, and thus variations on cometabolic degradation rate appeared to be much larger in comparison with the rates by the change of specific growth rate.

Taken together, it is very important to overcome limitations that cause our predictive model to underperform and consider the influence of model parameters. Although some

parameters were varied at different conditions, the variations of not only specific growth rate of AOB, but also microbial populations of AOB can play an important role in enhancing the cometabolic degradation. Consequently, the sensitivity analysis made this model more suitable for predicting cometabolic degradation of target compounds.

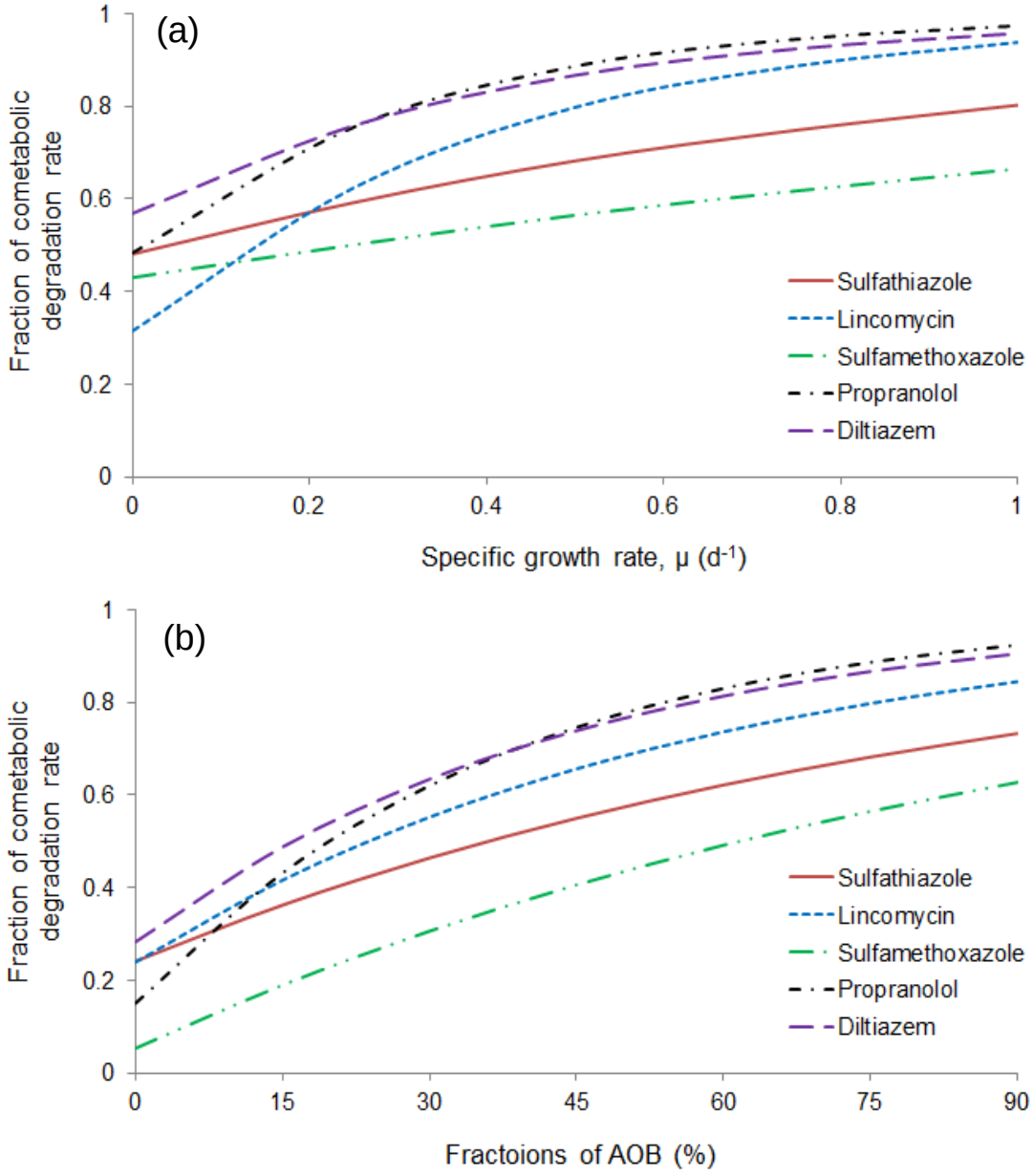


Figure 7.6 Prediction of cometabolic degradation rate for target compounds depending on the variations of (a) specific growth rate, μ and (b) fractions of AOB

7.4 Conclusions

In this chapter, model was developed to predict removal performance of PPCPs in MBR process based on the removal pathways, mainly biodegradation. Also, statistic tools were employed to not only identify correlations between observed and modelled results, but also investigate possible factors affecting the removal of PPCPs such as operating conditions of MBR process. Pilot-scale MBR process which was operated for 16 months, in which the applicability of predictive model for long-term operation was evaluated. Furthermore, cometabolic model predicted more accurately the removal by cometabolic degradation of several substances, in which model parameters affecting the performance of model were also taken into account. The main conclusions can be drawn as follows:

1) From the promising results of PCA, the correlations between operating conditions and removal of PPCPs was identified, in which biodegradation was positively dependent to temperature (e.g., ketoprofen, trimethoprim, diltiazem and diclofenac) and MLSS concentration (e.g., furosemide, naproxen, DEET, azithromycin and clarithromycin), but not significantly associated with DO level in the bioreactors and residual NO_3-N concentration in effluent.

2) For bezafibrate, ketoprofen, furosemide and naproxen, predictive model on removal performance showed a perfect match to observed data in pilot-scale MBR process, suggesting that this model can be practically applied in MBR process to predict elimination of compounds which have a higher biodegradability in accordance with conditions of microorganisms in the bioreactors

3) Compared with pseudo first-order kinetics, the proposed cometabolic model, with various parameters predicted more accurately the elimination caused by cometabolic degradation for some compounds (e.g., propranolol, diltiazem, sulfathiazole, sulfamethoxazole and lincomycin), in which the removal was attributed to the growth of AOB and biotransformation by nitrification.

4) Influence of model parameters which were overly susceptible to the change of microorganisms were evaluated, indicating that the variations of not only specific growth rate of AOB, but also microbial populations of AOB can play an important role in enhancing the cometabolic degradation.

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ChapterⅧ

Conclusions and Recommendations

8.1 Conclusions

Recently, one of the key issues in wastewater reclamation is the emerging problem of micropollutants such as PPCPs due to their potential to cause negative effects on aquatic ecosystems. The main source of these compounds has been known as the effluent from WWTPs, but current WWTPs operating usually by conventional biological treatment process are only designed for removal of organic matters and nutrients, without considering PPCPs, and thus most of these compounds are not completely removed. On the other hand, MBR process has become an alternative to CAS processes for removal of PPCPs in wastewater treatment since a higher MLSS concentration usually developed in MBR process can improve the biodegradation potential and adsorption capability, thereby ensuring not only the great removal of PPCPs, but also effective treatment of conventional pollutants. Even though many studies have focused on occurrence and removal of PPCPs, there is still little information on removal characteristics of PPCPs in MBR and comparative evaluation for efficient treatment processes. Furthermore, the reasons why MBR process can achieve efficient removal of these compounds have not been clearly revealed. Therefore, in this study, removal characteristics and mechanisms of PPCPs were investigated by performing batch experiments as well as field surveys of various WWTPs. The predictive model was also developed based on removal pathways of each compound, in which validation and sensitivity of the proposed model were evaluated using statistic tools and removal performance obtained in pilot-scale MBR process.

The main findings of this study are summarized below by each chapter.

In Chapter III, the occurrence of total 57 compounds were investigated, in which

acetaminophen, caffeine, naproxen and theophylline were observed at the highest level, and their mass loading rate including stimulant, NSAIDs, and antibacterials accounted for median 85% of all WWTPs. It was apparent that removal of PPCPs was mainly achieved in biological treatment process. Although removal of PPCPs under the conditions normally applied for disinfection was not observed, the removal performance of levofloxacin, mefenamic acid, sulfamethoxazole and furosemide in UV treatment and furosemide, carbamazepine and sulfapyridine in ozone treatment slightly increased. Moreover, from the results of comparison on fate and removal characteristics between MBR and various CAS processes, increased removal performance found in lab-scale MBR was attributed to enhanced biodegradation and adsorption tendency, in which the main removal routes were found to be biodegradation, whereas adsorption onto sludge was deemed to be a minor pathway except for some compounds with high adsorptive characteristics.

In Chapter IV, the study on combination of MBR and coagulation process was evaluated to mitigate membrane fouling and achieve efficient removal of both PPCPs and conventional pollutants. In the aspect of fouling control, permeability performance increased in accordance with addition of two coagulants (PAC and chitosan) and membrane fouling was significantly reduced due to the attenuated irreversible fouling by decrease of SMP concentration and inorganic materials of cake layer or membrane surface, whereas removal efficiency of PPCPs was much higher in injection of PAC than that of chitosan. Also, long-term operation was conducted using PAC, in which compared with control-MBR, removal of some PPCPs such as ketoprofen, diclofenac, furosemide and sulfamethoxazole was found to be effective in coagulation-MBR. It can be proven by the results on comparison of mass balance between two systems, suggesting that increased removal efficiencies could be mostly attributed to the enhanced biodegradability rather than adsorption onto sludge caused by coagulation or flocculation. This result would give useful insights into the applicability of combination of MBR and coagulation process in terms of control of membrane fouling and even efficient removal of PPCPs.

In Chapter V, batch experiments were carried out to elucidate the removal pathways in MBR process by determining the biodegradation and adsorption constant of 45 selected compounds according to different kinetic models. Estimated parameters including reaction constant, half-lives and normalized biodegradation rate were successfully determined, in which removal pathways of individual compounds were

significantly relevant to classes or categories of PPCPs. Biodegradation and adsorption onto sludge were considered as important factors for eliminating PPCPs, but the influence of hydrolysis and volatilization were negligible. The removal of NSAIDs, such as naproxen, ketoprofen and fenoprofen followed biodegradation kinetic model, in which significantly higher biodegradation rate was observed with MBR sludge. Antibiotics like azithromycin, roxithromycin and clarithromycin were removed by collaborative pattern between biodegradation and adsorption. Also, from the results of comparative evaluation between MBR and CAS sludge, the fate of persistent or non-degradable substances like furosemide, diclofenac, sulfathiazole and DEET in CAS moved from a recalcitrant behavior to a partial removal in MBR sludge, which can be attributed to enhanced biodegradation. Although it was found to be greater K_{bio} values in MBR for highly biodegradable compounds, with ranging from 1 to 10 $L/g_{VSS}.d$ (e.g., fenoprofen, bezafibrate, ketoprofen, and naproxen), some substances which more tended to adsorb onto sludge, with K_{bio} values ranging from 0.1 to 1 $L/g_{VSS}.d$ were found to be higher values in CAS. Lastly, elimination via adsorption was not strongly dependent on the sludge characteristics and thus, high MLSS concentration seems not to appreciably affect removal via adsorption onto sludge in MBR process.

In Chapter VI, removal of PPCPs by variations of SRT was investigated and the distinct capability of nitrifying bacteria to degrade target compounds was also evaluated. Removal of highly biodegradable compounds was not dependent on the variations of SRT, whereas some moderate or hardly biodegradable compounds, such as naproxen, indometacin, furosemide and DEET were significantly affected by increase of SRT. It means that MBR process operating at a prolonged SRT can obviously provide conditions more conducive to biodegradation of some PPCPs. The estimated cometabolic degradation rates and transformation yields indicated the influences of nitrification rate on the degradation of PPCPs, suggesting that the compounds having greater values are able to be highly degraded by cometabolism. Therefore, our study demonstrated why different removals were obtained in MBR process in terms of removal of PPCPs, in which both a prolonged SRT and variations of microbial community contributed to the enhanced removal of PPCPs in MBR process and thus, experimental results from batch tests would be valuable parameters for developing predictive models.

In Chapter VII, two different models were developed to predict effect of cometabolic degradation as well as removal performance of PPCPs based on the results of batch

experiments performed in Chapter V and VI. Firstly, the correlations between operating parameters and removal efficiency were assessed with PCA, in which temperature and MLSS concentration was significantly responsible for biodegradation of some substances. For bezafibrate, ketoprofen, furosemide and naproxen, predictive model on removal performance showed a perfect match to observed data in pilot-scale MBR process, suggesting that this model can be practically applied in MBR process to predict elimination of compounds which have a higher biodegradability in accordance with conditions of microorganisms in the bioreactors. Moreover, cometabolic degradation for five compounds like propranolol, diltiazem, sulfathiazole, sulfamethoxazole and lincomycin was verifiably predicted by the proposed cometabolic model. This model showed more accurate outputs in comparison to the pseudo first-order kinetics, where the removal of these compounds was attributed to the growth of AOB and biotransformation by nitrification. In addition, influence of model parameters which were overly susceptible to the change of microorganisms were evaluated, indicating that the variations of not only specific growth rate of AOB, but also microbial populations of AOB can play an important role in enhancing the cometabolic degradation. Consequently, two different models can be a beneficial tool in predicting removal performance of PPCPs in MBR process. Also, the predictive models with consideration for removal characteristics of target compounds could be put into practice.

8.2 Recommendations for future study

1) Additional batch studies on model parameters are recommended to investigate the effect of operating conditions like temperature on the removal of PPCPs in MBR process. In general, the variations of temperature contribute to promote biological activity of microorganisms, resulting in the efficient removal of target compounds. Also, specific concentration of AOB and HET were not experimentally measured. It is well known that the abundance of these compositions is very changeable in biological treatment process with operating at various conditions. Therefore, further study is needed to estimate the number of microbial composition for developing more accurate model on cometabolic degradation.

2) Our study focused on the enhanced removal characteristics of PPCPs obtained from advantages of MBR process, without considering the conjugated compounds or metabolites. However, they can be cleaved into the original parent compound during

biological treatment process, thereby negatively affecting the performance of microbial reaction. Hence, further study is recommended to understand the effect of conjugated compounds and metabolites to better predict removal fate and performance of PPCPs in MBR process.

Supporting information

Table S-1 Estimated parameters of biodegradation and adsorption between MBR and CAS

		CAS process								MBR process							
		Biodegradation				Adsorption				Biodegradation				Adsorption			
		Rate constant	Half-lives	K_{bio}	R^2	K_d (after 10h)	K_c	Normalized K_c	R^2	Rate constant	Half-lives	K_{bio}	R^2	K_d (after 10h)	K_c	Normalized K_c	R^2
		h^{-1}	h	$L/g_{VSS}\cdot d$		L/kg	h^{-1}	$L/g_{VSS}\cdot d$		h^{-1}	h	$L/g_{VSS}\cdot d$		L/kg	h^{-1}	$L/g_{VSS}\cdot d$	
1	Antipyrine	< 0				27.4				< 0		0.003		23.5			
2	Ketoprofen	0.008	86.0	0.229	0.91	33.0				0.280	2.5	0.587	0.91	24.5			
3	Naproxen	0.010	69.3	0.284	0.95	30.2				0.587	1.2	1.231	0.92	24.9			
4	Fenoprofen	0.091	7.6	2.756	0.99	50.3	0.041	1.173	0.96	1.228	0.6	3.435	0.99	36.8	0.030	0.064	0.96
5	Diclofenac	< 0				57.4				0.022	31.3	0.046	0.90	66.3			
6	Indometacin	0.001	488.9	0.040	0.75	59.2				0.033	20.9	0.069	0.93	77.1			
7	Mefenamic_acid	0.005	141.3	0.139	0.93	86.7				0.044	15.8	0.092	0.97	120.0			
8	Azithromycin	< 0				105.4				0.030	23.1	0.125	0.95	59.1	0.075	0.158	0.86
9	Tylosin	0.030	22.9	0.931	0.98	73.5	0.095	2.694	0.81	0.021	32.8	0.103	0.96	112.9	0.078	0.164	0.86
10	Clarithromycin	0.017	40.4	0.522	0.94	50.6	0.060	1.712	0.92	0.037	18.5	0.132	0.98	62.2	0.046	0.096	0.99
11	Roxithromycin	0.009	74.8	0.280	0.94	60.2				0.040	17.2	0.138	0.98	56.8	0.055	0.115	0.86
12	Tetracycline	0.003	220.2	0.089	0.85	3051.5				0.003	231.6	0.006	0.60	9167.9			
13	Oxytetracycline	0.003	216.8	0.091	0.70	2521.2				0.006	117.2	0.012	0.72	8707.6			
14	Thiamphenicol	<LOQ				27.6				<LOQ				15.4			
15	Trimethoprim	< 0				54.8				< 0				71.7			
16	Tiamulin	0.014	48.0	0.519	0.94	217.0	0.040	1.131	0.93	0.010	69.8	0.075	0.96	259.1	0.042	0.087	0.69
17	Sulfathiazole	< 0				31.2				0.013	54.4	0.027	0.99	26.5			
18	Sulfapyridine	< 0				36.0				0.004	187.7	0.008	0.48	25.0	0.027	0.057	0.76
19	Sulfamerazine	0.002	365.9	0.054	0.79	31.3				0.005	129.8	0.011	0.93	22.3			
20	Sulfadimidine	< 0				44.2				< 0				62.9			
21	Sulfamethoxazole	< 0				26.6				0.007	96.1	0.015	0.93	16.7			
22	Sulfamonomethoxine	0.002	362.5	0.054	0.69	28.9				0.003	230.7	0.006	0.47	19.0			
23	Sulfadimethoxine	0.005	152.4	0.129	0.15	27.6				0.006	120.7	0.012	-	48.9			
24	Levofloxacin	<LOQ				442.6				<LOQ				5330.0			
25	Norfloxacin	<LOQ				1098.2				<LOQ				5918.2			
26	Ciprofloxacin	<LOQ				1059.8				<LOQ				6906.3			
27	Atenolol	0.049	14.1	-	0.97	<LOQ				0.272	2.5	-	0.94	<LOQ			
28	Metoprolol	0.010	70.2	0.293	0.92	52.0				0.008	83.5	0.023	0.98	32.9			
29	Disopyramide	< 0				60.7				< 0				76.1			
30	Propranolol	< 0				376.5				0.004	162.7	0.071	0.74	655.3			
31	Diltiazem	< 0				85.9	0.033	0.935	1.00	< 0				99.9	0.097	0.202	0.99
32	Clofibric_acid	< 0				24.8				< 0				18.9			
33	Bezafibrate	0.041	16.8	1.207	0.99	29.6				0.813	0.9	2.070	0.74	26.2			
34	Theophylline	0.337	2.1	9.887	0.87	9.8				6.049	0.1	15.394	1.00	10.2			
35	Caffeine	0.217	3.2	6.410	0.98	5.1	0.075	2.120	0.98	5.513	0.1	27.979	1.00	13.2			
36	Furosemide	< 0				34.4				0.031	22.2	0.080	0.89	33.7			
37	DEET	0.003	275.5	0.071	0.90	36.5				0.041	17.0	0.109	0.74	26.3	0.022	0.045	0.88
38	2QCA	< 0				31.0				0.010	69.5	0.021	0.99	18.2			
39	Primidone	< 0				33.5				< 0				26.5			
40	Cyclophosphamide	0.002	330.0	0.060	0.79	32.8				< 0				21.4			
41	Carbamazepine	< 0				51.0				0.001	568.8	0.003	0.02	47.6			
42	Isopropylantipyrine	< 0				29.8				0.001	523.7	0.003	0.01	26.8			
43	Griseofulvin	0.002	295.2	0.071	0.91	59.5				0.012	59.1	0.036	0.98	54.4	0.112	0.236	0.83
44	Crotamiton	0.003	198.8	0.104	0.86	43.5	0.044	1.239	0.93	0.004	194.4	0.010	0.85	36.2	0.035	0.074	0.99
45	Pirenzepine	0.002	380.3	0.052	0.48	44.3				0.001	1140.9	0.001	-	39.7			

Table S-2 Estimated parameters of target compounds with and without AOB inhibition

		A1 (w/o AOB inhibition)				A2 (w/ AOB inhibition)			
		Rate constant	Half-lives	K_{bio}	R^2	Rate constant	Half-lives	K_{bio}	R^2
		h^{-1}	h	$L/g_{VSS} \cdot d$		h^{-1}	h	$L/g_{VSS} \cdot d$	
1	Antipyrine	<0				<0			
2	Ketoprofen	0.477	1.5	1.713	0.96	0.147	4.7	0.529	0.99
3	Naproxen	0.218	3.2	0.785	0.98	0.041	16.7	0.149	0.83
4	Fenoprofen	0.737	0.9	2.649	0.99	0.580	1.2	2.085	0.97
5	Diclofenac	0.025	27.8	0.090	0.98	0.013	55.4	0.045	0.93
6	Indometacin	0.068	10.2	0.244	0.99	0.023	30.2	0.082	0.99
7	Mefenamic_acid	0.020	34.8	0.072	0.94	0.003	249.6	0.010	0.72
8	Azithromycin	<0				<0			
9	Tylosin	<0				<0			
10	Clarithromycin	<0				<0			
11	Roxithromycin	<0				<0			
12	Tetracycline	<0				<0			
13	Oxytetracycline	<0				<0			
14	Thiamphenicol	<LOQ				<LOQ			
15	Trimethoprim	0.011	61.4	0.041	0.95	0.004	195.1	0.013	0.78
16	Lincomycin	0.022	32.2	0.077	0.87	0.011	60.6	0.041	0.93
17	Tiamulin	<0				<0			
18	Sulfathiazole	0.036	19.2	0.130	0.95	0.012	60.1	0.041	0.97
19	Sulfapyridine	0.015	45.5	0.055	0.99	0.003	237.1	0.011	0.78
20	Sulfamerazine	0.015	46.4	0.054	0.97	0.001	509.2	0.005	0.83
21	Sulfadimidine	<0				<0			
22	Sulfamethoxazole	0.031	22.4	0.111	0.99	0.002	303.2	0.008	0.91
23	Sulfamonomethoxine	0.019	36.1	0.069	0.99	0.002	423.4	0.006	0.82
24	Sulfadimethoxine	0.018	37.7	0.066	0.68	0.005	148.9	0.017	0.41
25	Levofloxacin	<0				<0			
26	Norfloxacin	<0				<0			
27	Ciprofloxacin	<0				<0			
28	Atenolol	0.603	1.1	2.168	0.86	0.389	1.8	1.399	0.97
29	Metoprolol	0.223	3.1	0.801	0.99	0.049	14.2	0.176	0.94
30	Disopyramide	<LOQ				<LOQ			
31	Propranolol	0.073	9.6	0.260	0.92	0.007	101.7	0.024	0.58
32	Diltiazem	0.071	9.7	0.256	0.98	0.014	49.8	0.050	0.86
33	Clofibric_acid	0.006	110.7	0.022	0.97	0.002	461.9	0.005	0.59
34	Bezafibrate	0.257	2.7	0.924	0.99	0.155	4.5	0.557	0.97
35	Theophylline	1.386	0.5	4.978	0.92	1.390	0.5	4.995	0.91
36	Caffeine	0.964	0.7	3.462	0.92	1.523	0.5	5.473	0.96
37	Furosemide	0.226	3.1	0.814	0.99	0.024	28.3	0.088	1.00
38	DEET	0.006	113.9	0.022	0.88	0.004	180.6	0.014	0.76
39	2QCA	0.019	36.2	0.069	0.96	0.003	265.0	0.009	0.79
40	Primidone	<0				<0			
41	Carbamazepine	<LOQ				<LOQ			
42	Isopropylantipyrine	0.006	116.8	0.021	0.78	0.001	683.6	0.004	0.38
43	Griseofulvin	<0				<0			
44	Crotamiton	0.002	296.4	0.008	0.82	0.001	729.8	0.003	0.42
45	Pirenzepine	<LOQ				<LOQ			

<0: not available value by incorrect mass balance and <LOQ: limit of quantification.

Table S-3 Predicted and observed values for removal performance

PPCPs	Predicted values			Observed values		
	Adsorp. (%)	Biodeg. (%)	No rem. (%)	Adsorp. (%)	Biodeg. (%)	No rem. (%)
BZF	0 (0 – 1)	117 (98 – 131)	-17 (-31 – 2)	0 (0 – 7)	97 (92 – 99)	2 (1 – 5)
KTP	0 (0 – 1)	102 (86 – 115)	-3 (-15 – 14)	0 (0 – 1)	97 (87 – 99)	3 (1 – 12)
IDM	12 (0 – 102)	22 (19 – 25)	66 (-25 – 78)	2 (0 – 7)	46 (-6 – 75)	52 (25 – 103)
CAM	4 (0 – 26)	37 (31 – 42)	58 (43 – 67)	1 (0 – 2)	86 (13 – 96)	14 (4 – 85)
AZM	63 (0 – 214)	15 (12 – 17)	22 (-128 – 86)	2 (0 – 5)	84 (-13 – 98)	15 (2 – 110)
DTZ	9 (0 – 22)	63 (54 – 72)	28 (14 – 41)	3 (1 – 5)	49 (30 – 82)	48 (17 – 122)
FSM	5 (0 – 8)	79 (75 – 100)	17 (-1 – 25)	1 (0 – 3)	75 (63 – 99)	26 (0 – 37)
NPX	2 (0 – 8)	72 (42 – 77)	26 (16 – 57)	1 (0 – 4)	73 (43 – 78)	27 (18 – 55)

Adsorp.: Adsorption, Biodeg.: Biodegradation and No rem.: No removal.

Also, minimum and maximum values are given in brackets.