COMBINED CHLORINATION AND NANOFILTRATION TO ENHANCE REMOVAL EFFICIENCIES OF SULPHONAMIDE IN SIMULATED WASWATER

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ABSTRACT

Rapid advancement in healthcare and manufacturing industries has resulted in the introduction of new potentially harmful chemicals such as endocrine disrupting chemicals (EDCs) and pharmaceutically active compounds (PhACs) from wastewater produced by these industries into the water bodies. Presence of these types of compound at the final stages of the water treatment system may potentially render the disinfection process ineffective due to the formation of dangerous by-products that have higher toxicity compared to their parent compounds. In this study, the effectiveness of a system that combined two methods of treatment, namely chlorination and nanofiltration was compared with the conventional treatment method where the two systems are separately employed. Four types of sulphonamide derivatives (sulfanilamide (SNM), sulfadiazine (SDZ), sulfamethoxazole (SMX), and sulfadimethoxine (SDM)) were chosen as EDCs model. Sulphonamide is a synthetic antibiotic that is widely used by human as veterinary medicine especially in poultry farming. Using benchscale nanofiltration system, nanofiltration experiments were conducted in three different modes; 1) Pre-chlorination system where the Free Active Chlorine (FAC) was added to the membrane influent (i.e. chlorination followed by nanofiltration), 2) Post-Chlorination system where the FAC was added to the membrane effluent (i.e. chlorination after nanofiltration), and 3) Simultaneous system where the chlorination was subjected to the membrane feed during nanofiltration process (simultaneous chlorination and nanofiltration). Chlorination of sulphonamide at three different pH yields different reaction rates that varied greatly with pH 5.6 showing the highest rate compared to pH 7.2 and pH 10. From the first order plot of chlorination kinetics, the reactivity of sulphonamide with free chlorine is SDM > SNM > SMX > SDZ. Rejection rate for nanofiltration of sulphonamide derivatives without the presence of FAC are 12.5%, 69.5%, 75.5%, and 79.0% for SNM, SDZ, SMX, and SDM, respectively. Overall,

removal efficiencies of sulphonamide for pre-chlorination-nanofiltration system (>99.5%) and simultaneous system (>99.0%) are higher compared to the conventional nanofiltration-post-chlorination system (>89.5%). However, in the case of limited FAC ($[FAC]_0$: $[sulphonamide]_0 \leq 1$), removal efficiency for nanofiltration-post-chlorination system was higher compared to the other two systems due to the prior nanofiltration process that effectively removed 12.5% to 80% of four sulphonamide derivatives and consequently helped reduced the concentration of sulphonamide in permeate. Nanofiltration of reaction by-products in pre-chlorination and hybrid systems showed better results compared to post-chlorination system. Majority of the reactions by-products formed during the chlorination of sulphonamide were found to be higher in molecular weight compared to its original compound although some of the by-products size were smaller than the molecular weight cut-off (MWCO) of nanofiltration membrane employed. The flux for both pre-chlorination and hybrid systems were considerably higher than in the untreated feed system due to the reduction in the concentration of sulphonamide in membrane feed. Continuous exposure of membrane surface to FAC in both hybrid and pre-chlorination system contributed significantly to the increases of permeate flux. The rejection rates of Na^+ on used membranes suggest that the membrane used in pre-chlorination system was only slightly degraded from the chlorine attack. FTIR analysis and morphology study on membrane used in simultaneous system indicates that the membrane is significantly damaged.

ABSTRAK

Kemajuan pesat dalam industri pembuatan dan produk penjagaan kesihatan telah mengakibat pendedahan bahan kimia baru yang berbahaya seperti kimia perencat sistem endokrin (EDCs) dan sebatian aktif farmaseutikal (PhACs) dari sisa kumbahan dan buangan yang dihasilkan oleh industri-industri tersebut kedalam sumber air. Kewujudan sebatian ini dalam peringkat terakhir sistem rawatan air boleh menyebabkan proses pembasmian kuman menjadi tidak berkesan kerana pembentukan produk perantara yang lebih toksik daripada produk asal. Dalam kajian ini, keberkesanan sistem yang menggabungkan dua kaedah rawatan iaitu pengklorinan dan nanopenurasan telah dibandingkan dengan sistem rawatan konvensional di mana dua sistem kedua-dua sistem tersebut berfungsi secara berasingan. Empat jenis terbitan sulphonamide (sulfanilamide, sulfadiazine, sulfamethoxazole, and sulfadimethoxine) telah dipilih sebagai model EDCs. Sulphonamide adalah antibiotik sintetik yang digunakan secara meluas oleh manusia untuk perubatan veterinar terutamanya dalam bidang penternakan. Dengan menggunakan sistem nanopenurasan berskala makmal, eksperimen nanopenurasan telah dilakukan dalam tiga kumpulan mod berbeza iaitu: 1) sistem pra-pengklorinan di mana klorin aktif ditambah ke dalam aliran influen membran (iaitu pengklorinan diikuti oleh nanopenurasan), 2) pasca-pengklorinan di mana klorin aktif ditambah ke dalam aliran efluen membran (iaitu pengklorinan selepas penurasan nano), dan 3) sistem serentak di mana proses pengklorinan dilakukan kepada suapan membran semasa proses penurasan sedang berlaku (pengklorinan serentak dengan penurasan nano. Pengklorinan sulphonamide pada tiga pH yang berbeza menunjukkan kadar tindak balas yang sangat ketara di mana pH 5.6 adalah menunjukkan kadar tindak balas yang tertinggi berbanding dengan dua pH lain iaitu pH 7.2 dengan pH 10.0. Dari plot tertib pertama bagi kinetik pengklorinan, kereaktifan sulphonamide terhadap klorin aktif dari susunan paling reaktif ke paling kurang reaktif adalah SDM > SNM > SMX > SDZ.

Kadar penyingkiran untuk nanopenurasan bagi sulphonamide tanpa menggunakan klorin adalah sebanyak 12.5%, 69.5%, 75.5%, dan 79.0% bagi SNM, SDZ, SMX, dan SDM. Secara kesuluruhannya, sistem prapengklorinan-nanopenurasan (>99.5%) dan sistem serentak (>99.0%) menunjukkan keberkesanan penyingkiran yang lebih tinggi berbanding dengan sistem konvensional nanopenurasan-pascapengklorinan (>89.5%). Walaubagaimanapun, dalam kes di mana kuantiti klorin aktif adalah terhad, keberkesanan penyingkiran untuk sistem nanopenurasan-pascapengklorinan adalah lebih tinggi berbanding dengan dua sistem lain kerana proses nanopenurasan yang terdahulunya telah berjaya menyingkirkan 12.5% hingga 80% kandungan sulphonamide dan secara langsung membantu mengurangkan kepekatan sulphonamide yang meresap ke ruang permeasi. Nanopenurasan untuk produk hasil sampingan tindak balas bagi sistem pra-pengklorinan dan sistem serentak menunjukkan penyingkiran yang lebih baik berbanding dengan sistem pasca-pengklorinan. Majoriti daripada produk hasil sampingan tindak balas proses pengklorinan untuk sulphonamide adalah didapati bersaiz molekul yang lebih besar berbanding dengan kompaun yang asal walaupun ada sebahagiannya adalah lebih kecil daripada saiz liang membran nanopenurasan (MWCO). Kedua-dua fluks bagi sistem pra-pengklorinan dan sistem serentak adalah jauh lebih tinggi berbanding dengan sistem di mana suapan membrannya yang tidak dirawat kerana penurunan kepekatan sulphonamide di dalam suapan membrane. Pendedahan klorin aktif yang berterusan kepada permukaan membran dalan kedua-dua sistem prapengklorinan dan gabungan turut menyumbang kepada peningkatan yang jelas kepada fluks. Berdasarkan kepada kadar penurasan Na^+ menggunakan membran yang sama selepas eksperiment menunjukkan yang membran dalam sistem prapengklorinan tidak rosak hasil dari tindak balas klorin. Akan tetapi, analisa FTIR dan kajian ke atas permukaan membran yang digunakan dalam sistem serentak menunjukkan bahawa membran rosak dengan ketara.

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AS	:	Activated Sludge
BPA	:	Bisphenol A
CAS	:	Conventional Activated Sludge
CDL	:	Curved Desolvation Line
Cl_2	:	Chlorine
Da	:	Dalton
DBP	:	Disinfection By-Product
DEHP	:	Di(2-ethylhexyl) Phthalate
DN	:	Denitrification
EDCs	:	Endocrine Disrupting Chemicals
FAC	:	Free Active Chlorine
FESEM	:	Field Emission Secondary Electron Microscopy
FTIR	:	Fourier Transform Infrared Spectroscopy
HAA	:	Haloacetic Acid
HOCl	:	Hypochlorous Acid
HPLC	:	High Performance Liquid Chromatography
LC-TOF-MS	:	Liquid Chromatography-Time of Flight-Mass Spectrophotometer
M	:	Molar
MWCO	:	Molecular Weight Cut-Off
NF	:	Nanofiltration
NH_4Cl	:	Ammonium Chloride
NOM	:	Natural Organic Matter
OCl^-	:	Hypochlorite Ion
PFCs	:	Perflourinated Chemicals
PhACs	:	Pharmaceutically Active Compounds
pKa	:	Acid Dissociation Constant
PPCPs	:	Pharmaceuticals and Personal Care Products
PPM	:	Part per Million
PT	:	Primary Treatment
RO	:	Reverse Osmosis
SCP	:	Sulfachloropyridazine
SCT	:	Sulfacetamide
SDM	:	Sulfadimethoxine
SDZ	:	Sulfadiazine
SMT	:	Sulfamethazine
SMX	:	Sulfamethoxazole
SNM	:	Sulfanilamide
SNs	:	Sulphonamide
STZ	:	Sulfathiazole
T	:	Temperature
TEDX	:	The Endocrine Disruption Exchange (TEDX)
TF	:	Trickling Filter
THAM	:	Tris(Hydroxymethyl) AminoMethane
THM	:	Trihalomethane
TMP	:	Transmembrane Pressure
UV	:	Ultraviolet
V	:	Volume

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CHAPTER 1

INTRODUCTION

1.1 Research Background

The pursuit of higher quality of life, including healthy lifestyles and the treatment of debilitating diseases have created demands for more sophisticated products, such as hormones and new pharmaceutical chemicals. While the technology to manufacture such products has progressed in tandem, there are concerns regarding the input of these new chemicals and its metabolites into the water environment from various sources. The presence of these micropollutants could introduce a negative impact on the water quality and caused harmful effects on humans. One of the potentially harmful groups of chemical that is being introduced into the environment is endocrine disrupting chemicals (EDCs) (Balabanič et al., 2011; Natural Resources Defense Council, 2012). EDCs are substances that interfere with the functioning of hormone systems in human and wildlife resulting in negative response of endocrine system.

The occurrences of EDCs in surface water are well documented. For example, (Luo et al., 2014) reported that estrogen ranging from 0.98 to 21.6 ng/L were detected in three rivers of Tianjin, China. Furthermore, high frequencies of perflourinated compound (PFCs) were detected in multiple sections of Langat river basin, in Malaysia (Zainuddin et al., 2012). Leachate from landfill sites with improper disposal of drugs of medicine may also contribute to the presence of EDCs in surface water.

EDCs are also frequently detected in treated water such as tap water and bottled water. Analysis done by Thompson et al. (2011) reported that up to 16 ng/L concentration of EDCs was detected in tap water. Another study by Li et al. (2010) also shows the presence of EDCs in tap water/bottled water in China with concentration ranging from 108 ng/L to 298 ng/L. In Kuala Lumpur, Malaysia, BPA concentration as high as 59.8 ng/L and 11.3 ng/L were observed in tap water and bottled water respectively (Santhi et al., 2012). EDCs in treated water are likely to come from the water pipes during water distribution to household or may also come from the bottle itself.

Generally, the conventional water and wastewater treatment techniques do not effectively remove these micropollutants (Janex-Habibi et al., 2009; Klaus, 2009). Various studies conducted on the removal of micropollutants such as EDCs via conventional water treatment plants showed incomplete removal, which is mainly due to the limited degradability of these micropollutants, combined with low concentrations detected in the surface water (sub ng/L) (Huerta-Fontela et al., 2011; Rivera-Utrilla et al., 2013). For example, even with the 90% removal efficiencies in treatment plant in China, a residual of 2.38 ng/L and 14.2 ng/L of DBP and DEHP were still detected in the effluent respectively (Deblonde et al., 2011). A more advance treatment method is required to increase the removal efficiencies of EDCs in water and wastewater treatment plants. Membrane separation technology, such as nanofiltration and reverse osmosis, is increasingly employed for the removal of PhACs and EDCs. Nanofiltration and reverse osmosis have the ability to remove low molecular weight organic contaminants, including the disinfection by-products (Al-Rifai et al., 2011; Radjenović et al., 2008). Nanofiltration as one of the best treatment methods currently available to improve the water effluent of treatment plants is considered to be used in this study.

1.2 Problem Statement

In a normal water and certain wastewater treatment plant, chlorination process or widely known as disinfection is a must. Due to the strict drinking water quality standard set by the Department of Environment, Malaysia especially on pathogen residual, it is compulsory for every water treatment plant in Malaysia to conduct disinfection process prior to water distribution (Ministry of Natural Resources and Environment, October 2010). Disinfection is necessary in order to kill residual pathogen and thus preventing the dangerous pathogens from reaching the end user pipeline.

However, an increased number of organic micropollutants that are present in the water and wastewater effluent due to incomplete removal have rendered the disinfection process in the treatment plants ineffective which has repercussion on treated water (Chen et al., 2008). The situation is further complicated by the presence of dangerous by-products from the reaction between disinfectants and micropollutants (Shen & Andrews, 2011). Nevertheless, it is also acknowledged that the disinfection process is imperative to ensure the safety of treated water quality, and cannot be simply removed from the treatment process. In order to address this emerging problem, other alternative modes of treatment system, such as membrane process, needs to be examined, so as to eliminate or reduce the concentration of organic micropollutants during the existing disinfection process.

Membrane filtration is a promising technology in removing EDCs and PhAC in water and wastewater treatment plant (Dolar et al., 2011; Plakas & Karabelas, 2012). However, membrane filtration has a few disadvantages. Membrane processes lack the ability to destroy organic pollutants, and as a result of this, rejected pollutants will

accumulate in the retentate, which will require the disposal of the pollutants in the retentate stream. Moreover, the membrane is prone to fouling after continuous long-term operations, due to the presence of suspended particles and colloidal material in the membrane feed (Van der Bruggen et al., 2008; Verlicchi et al., 2009).

A possible simultaneous solution to both of these problems is to devise a process that treats the feed to the membrane process. Chlorination, although mainly used as a disinfectant, may also be considered as pre-treatment prior to the membrane process. Chlorine is capable of degrading EDCs, but it is not independently suitable for water treatment, due to the potential formation of harmful by-products (Esplugas et al., 2007). However, these dangerous compounds that are formed during chlorination could effectively be removed by combining the process with membrane filtration (Ates et al., 2009; Lin et al., 2006). Moreover, the presence of chlorine in the membrane feed could help reduce membrane fouling by partially cleaning the membrane's surface (Kang et al., 2007). This proposed combination process might be able to balance the advantages and disadvantages of the nanofiltration and chlorination process.

Following this proposal, the main question that came up is the determination of the mode of operation of this combined system that will give the best performance in terms of fluxes and rejection of micropollutants, together with its by-products: i.e. Pre-chlorination or Post-chlorination with respect to the membrane stage. This research aims to compare the removal efficiencies (flux and micropollutants removal) of organic micropollutants between two different modes that employ the addition of free chlorine at different stages during the nanofiltration process. In this study, an antibiotics compound sulphonamide is chosen as the EDCs representative. From the previous studies conducted on the analysis of pollutant in selected Malaysian river basin,

sulphonamide is one of the highest micropollutants detected (Malintan & Mohd, 2006). Combined with unique characteristic of sulphonamide, where one of the chlorination by-products is able to retransform to the parent compound in the absence of the chlorine agent makes sulphonamide an interesting compound for this study. Furthermore, one of the sulphonamide chlorination by-products was also found to be more toxic compared to their respective parent compound. Four types of sulphonamide derivatives were used namely, sulfanilamide, sulfadiazine, sulfamethoxazole, and sulfadimethoxine.

1.3 Objectives of the Study

The central treatment is based on nanofiltration. However a hybrid system is proposed which involves chlorination. The chlorination stage is combined with nanofiltration in three (3) different modes.

i. Chlorination followed by nanofiltration

ii. Chlorination after nanofiltration

iii. Simultaneous chlorination and nanofiltration

The objectives are:

- To compare the effectiveness between the above systems in terms of rejections of all four sulphonamide derivatives and fluxes performances of nanofiltration.
- To study the effect of chlorine exposure to membrane characteristics.

1.4 Scope of Study

This study focuses on the combination of chlorination and nanofiltration in the removal process of EDCs in water. The main point used for comparison between the studied systems will be in terms of rejections and fluxes performance during nanofiltration resulting from the application of chlorine. This study only focuses on one type of EDCs, which is sulphonamide. In this work EDC is represented by its sulphonamide derivatives namely sulfanilamide, sulfadiazine, sulfamethoxazole, and sulfadimethoxine because it is constantly being detected in Malaysian surface water.

Sodium hypochlorite was used as the chlorine agent because it is easily available and much safer to use compared with chlorine gas. Nanofiltration membrane was chosen for this study due to its low energy requirement and ability to operate at lower cost compared to reverse osmosis membrane.

Prior to the study on the hybrid system, a preliminary study on the kinetic behavior of sulphonamide during chlorination process was performed. The effect of pH and the reactivity of chlorination process towards sulphonamide were the focus of this preliminary study. This preliminary study is deemed necessary in order to observe their effect on nanofiltration process resulted from the chlorination of sulphonamide.

1.5 Structure of Thesis

This thesis is divided into 5 chapters with each chapter covering the various parts. Chapter 1 briefly explains the background and purpose of this research. The objectives, together with the scope of studies are also covered in detail in this section.

Chapter 2 is mainly focused on the collection of available and published information relevant to the research that is being conducted. It starts with the introduction about micropollutant followed by the specific type of micropollutant which is Endocrine Disrupting Chemicals (EDCs) and then focused into compound of interest, sulphonamide. Most of the previous studies done on the treatment of EDCs and sulphonamide from water and wastewater are covered in this part. The literature about chosen treatment method in this research, which is a combination between nanofiltration and chlorination were collected and presented in this chapter.

Chapter 3 covers each part of the procedures and methods that were used to conduct the research and to collect the data. Properties of the studied compound and the characteristic of the membrane used are also presented in this section. Methodology for analysis using analytical equipment was adopted from published material.

Chapter 4 covers all the experimental data that were collected from this research. The discussion on the results started with the calibration of the analytical equipment followed by the preliminary study on the effect of chlorination process to the degradation of sulphonamide antibiotic. Combination between nanofiltration and chlorination, the main focus of this study are explained in details in the later part of the chapter. Comparison was done between all of the treatment modes involved in order to determine the most effective method to treat sulphonamide.

Chapter 5 summarizes the results and discussions explained in Chapter 4. Achievements of the objectives set out in this study are also concluded in this part together with a few recommendations that can improve the research in the future.

1.6 Significant of the Study

The data obtained from this study helps in understanding the ability of the membrane to reject not only the main compound sulphonamide but also all the by-products produced from the chlorination process. Study on the behavior of the sulphonamide in the presence of chlorine is important in identifying what kinds of by-products are produced from the reaction. The highlight of this research is the determination of the best method to treat sulphonamide using membrane in combination with the existing disinfection process in water and wastewater treatment plant.

CHAPTER 2

LITERATURE REVIEW

This chapter reviews the available literature on four relevant topics of this research namely; 1) Organic Micropollutants with special focus on Endocrine Disrupting Chemicals in general context, 2) Sulphonamide, which is the compound of interest in this research, 3) Membrane filtration system particularly nanofiltration system which is used in this study to remove sulphonamide compound, and 4) Disinfection system for water treatment focusing on chlorination process only.

2.1 Organic Micropollutants

Technology is advancing very rapidly and industries such as healthcare and manufacturing are trying very hard not to be left behind. As a result the volume of sewage and wastewater that are introduced from these industries to the environment also increases in tandem. Without an adequate treatment, these contaminants would likely end up in important water bodies such as surface and ground waters. Some of these micropollutants are not easily metabolized and have a high resistivity towards degradation. Excess organic micropollutants that resist degradation will mostly enter the aquatic environment and would likely interact with the aquatic living and directly affect the ecosystem thereby promoting drug-resistant microorganisms or even contaminating the source of food in aquatic ecosystems. One of the potentially harmful micropollutants that are being introduced into the environment is endocrine disrupting chemicals

(EDCs) (Balabanič, et al., 2011; Diamanti-Kandarakis et al., 2009; Natural Resources Defense Council, 2012).

Endocrine Disrupting Chemicals (EDCs) are substances that interfere with the functioning of hormone systems resulting in unnatural responses. The U.S. Environmental Protection Agency (2011) defined EDCs as "an exogenous agent that interferes with synthesis, secretion, transport, metabolism, binding action, or elimination of natural blood-borne hormones that are present in the body and are responsible for homeostasis, reproduction, and developmental process." The definition of EDC as stated above means compounds that have potential in triggering the endocrine system of organisms and causing adverse effects in the system. The next section will discussed the mechanism on how EDCs disrupt the function of endocrine system and their effect to human health. The monitoring studies done on EDCs together with the current technologies employed in removing these types of compound from the environment will also be discussed in the following section.

2.1.1 Mechanism of EDCs

There are two main mechanisms in which EDCs affect the endocrine system. EDC may act as: 1) Agonistic effect where EDCs mimic the hormone and binds to receptor in the cell, triggering either excessively of insufficiently the endocrine function or 2) Antagonistic effect where EDCs act as a blocker and blocks the hormone receptor, thus blocking the endocrine function. Figure 2.1 illustrates the general mechanism of receptor-mediated actions of endocrine disruptors on endocrine cell function.

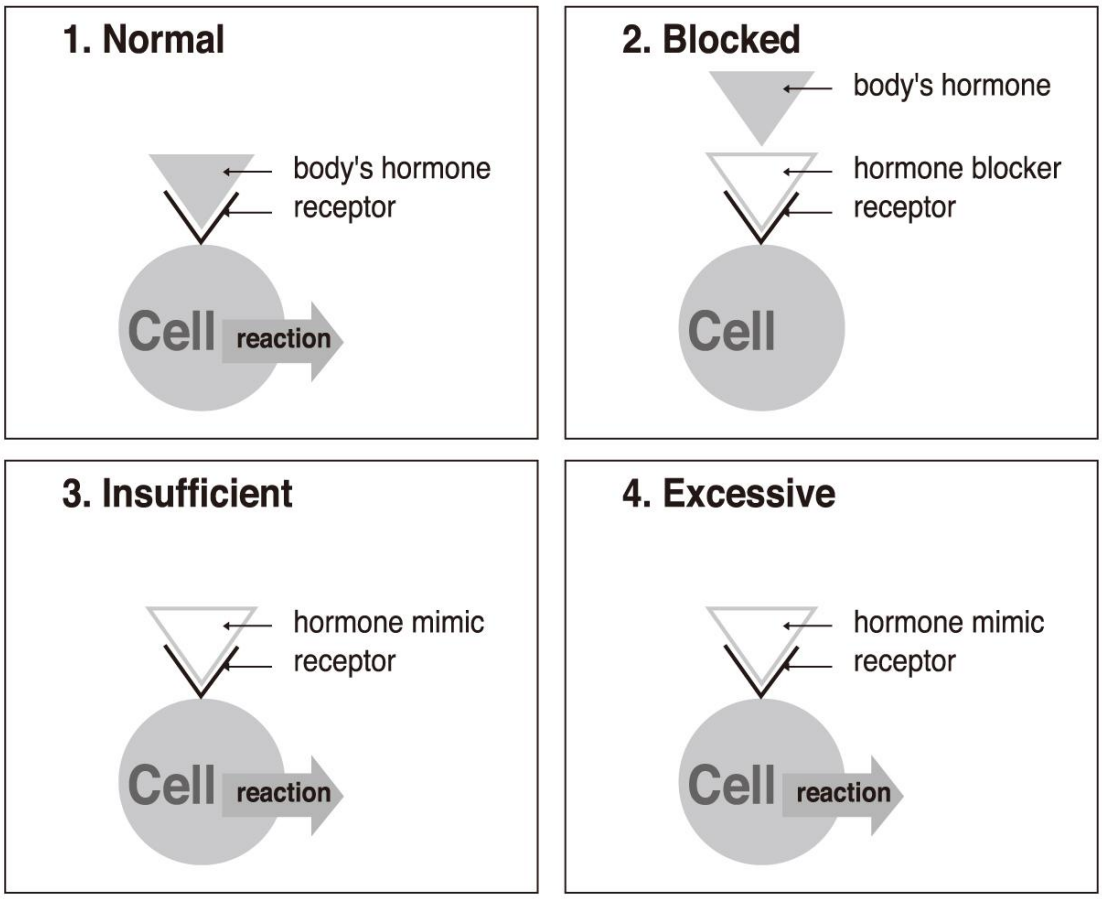


Figure 2.1: Mechanism of receptor-mediated actions of endocrine disruptors
(Source: Chang et al., 2007)

EDCs can also act as an endocrine flusher where the EDCs speed up the breakdown of natural hormore which resulted to the elimination of natural hormones from the body (Birkett & Lester, 2002).

Multiple research have connected endocrine disrupting chemical to the cancer, diabetes, obesity and infertility in human (Balabanič, et al., 2011; Caserta et al., 2008; De Coster & van Larebeke, 2012). For instance, Bisphenol A (BPA) has shown to cause infertility in male reproductive system where the number and quality of sperm reduced from exposure to BPA (Rochester, 2013; Schiffer et al., 2014). A study on the effect of EDC to cancer showed that the rate of testicular cancer across northern Europe increased exponentially in the past decade (Richiardi et at., 2004).

Beside human, growing evidence suggests that EDCs can also induce similar disruption in sexual development of aquatic wildlife (Bhandari et al., 2014; Diamanti-Kandarakis et al., 2009). For example, studies with alligators have confirmed that EDCs may responsible in decreased testosterone and smaller phallus size in males (Bhandari et al., 2014).

The systems that are affected by EDC mostly include all hormonal function especially from those controlling the development and function of reproductive organ.

2.1.2 Sources of EDCs

EDC can either come from natural plant-based like phytoestrogen from soy or man-made chemical like Bisphenol A. It is consist of several types of compounds such as organic, pesticides, hormones, drugs and their potential sources to environment are different depending on their application. Further details on different type of EDCs and their potential sources are listed in Table 2.1. Industrial discharge or effluent, agricultural runoff, excretion, leachate from dumpsite, and disposal of household drugs are among the top potential sources of EDCs in the water. On the other hand, a proportion of unmetabolized drugs may excrete out of human body and enter into the sewage system. Furthermore, landfill leachate may contain unwanted drugs or medicines that are disposed as household wastes. All these potential sources of EDCs are likely to end up in water bodies.

Table 2.1: Category of EDCs and its potential sources
(Source: Birkett & Lester, 2002; Bolong et al., 2009; Chang et al., 2009; Chung Zie Wei, 2007; Kanematsu et al., 2009)

Category	EDC	Uses	Potential Sources
Organic	Bisphenol A	Epoxy resin and plasticizer in plastic	Leachate from dumpsite Industry effluent
	Pthalates		
Pesticides	Lindane	Organochlorine pesticide, fungicide, insecticide to prevent, eliminate and ward off pest	Leachate from dumpsite Domestic sewage effluent Industry effluent Agriculture runoff
	HCB		
	Mirex		
	Endrine		
	Dieldrin		
	DDE		
	DDT		
	DDD		
	Heptaclor		
	Endosulfan		
Alkylphenols	Nonylphenol	Detergents, Surfactant, capacitors and, transformer	Leachate from Dumpsite Domestic sewage effluent Industry effluent
	Octylphenol		
	PAH		
	PCB		
Drugs, Hormone and Antibiotics	17-β-estradiol	Human and animal Antibiotics, Stimulant	Leachate from dumpsite Domestic sewage effluent Industry effluent
	Diethylstilbestrol		
	Estrone		
	Ethynyl estradiol		
	Sulphonamide		
	Chloramphenicol		
	Tetracylines		
Others	Dioxin	Bleaching	Leachate from dumpsite Domestic sewage effluent
	Furan	-	
	Tributyltin	Paint additive	
	Parabens	Preservative	
	Musk xylol	Fragrance	

2.1.3 EDCs Studies in Malaysia

One of the earliest works on monitoring and health impact assessment of EDCs in Malaysia was initiated by Professor Dr. Mustafa from the Department of Pathology, University Malaya who is now a pioneer in this field (Tan & Ali Mohd, 2003; Tan et al., 2003; Tan & Mustafa, 2003). His research team focuses on the detection and effects of various EDCs found in Malaysian environment including surface water, blood and also foods to animals and human. Various articles have been published by this team, and some of the results show that EDCs have impacts not only on animals but on humans as well. For example, a study on exposure of bisphenol A (BPA) and nonylphenol to the pubertal development and thyroid function in male rats by Tan et al. (2003) confirmed that EDCs is in fact harmful to the rats. BPA was found to cause kidney enlargement to the tested rats. Furthermore, testicular damages and significant delay in puberty were also observed in the rats.

An antibiotics monitoring program done by Malintan & Mohd (2006) on three states river (Perak, Melaka, and Selangor) also found that 103 out of 300 samples collected were found positive for sulphonamide. Concentrations between 5 ng/L to 95 ng/L of sulphonamide were detected. Another analysis conducted in the Sungai Selangor showed that bisphenol A, phthalates and various types of pesticides were present in the water (Santhi & Mustafa, 2012). Although these compounds were detected at trace levels, the persistent characteristic of these compounds might impact the water quality in the near future. Perflourinated compound (PFCs) as an emerging pollutant is also gaining interest to Malaysian researchers. A recent analysis of that compound by Zainuddin et al. (2012) from Universiti Kebangsaan Malaysia showed that high

concentrations of PFCs were detected in Sungai Langat (ppb level). Table 2.2 shows the summary of concentration of EDCs found in Malaysian river basin in the past years.

Table 2.2: Current concentration of Endocrine Disrupting Chemicals (EDCs) in Selected Malaysia river basin.

Type of EDC	Compound	Location	Year	Highest Concentration Detected (ng/L)	Reference
Pesticides	Lindane	River in Selangor Area	2012	24.6	Santhi & Mustafa (2012)
	HCB			3.4	
	Mirex			4.6	
	Endrine			2.0	
	Dieldrin			8.0	
	p,p' DDE			2.7	
	p,p' DDD			4.8	
	p,p' DDT			6.2	
	Chlorpyrifos		2003	195.2	Leong et al. (2007)
	Heptaclor			239.1	
	Endosulfan			1848.7	
	Diazinon			510.0	
	Endosulfan sulfate		2002	192.1	Tan & Mustafa (2004)
Antibiotics	Sulphonamide	Perak	2005	93.75	Malintan & Mohd (2006)
		Melaka		94.15	
		Selangor		94.95	
	Chloramphenicol	Perak	2005	264,040	
		Melaka		176,260	
Organic	Bisphenol A	Selangor	2012	215	Santhi et al. (2012)
	Phthalates		2012	507.4	Santhi et al. (2012)
	PFOA	Sungai Langat	2010	5940	Zainuddin et al. (2012)
	PFOS			87620	

2.1.4 Current Technologies for Removal of EDCs

The efficiencies of EDCs removal are varied depending on method employed during the treatment processes and type of water matrixes. For example, 55% of Bisphenol A (BPA) were removed from water using sonochemical degradation (Pétrier et al., 2010) compared to 94% removal using ultrasonic (Gültekin & Ince, 2008). In addition, ozonation of BPA in ultrapure water showed completed removal (Deborde et al., 2008) while about 61% of BPA were removed in wastewater (Snyder et al., 2006). This suggests that a proper treatment process need to be cautiously selected in accordance to the unique characteristic and properties of different EDCs and also the type of water sources. Table 2.3 summarizes the efficiencies of EDCs removal from water and wastewater by various physiochemical treatments for the past few years. The removal of multiple EDCs using powdered activated carbon (PAC) and chlorination in water by Westerhoff et al. (2005) shows that more than 90% of EDCs were found to be successfully removed by using this method. Among all the treatment methods available today, advanced water treatment such as advance oxidation process (ozonation and chlorination) was also found to show promise in eliminating EDCs in both water and wastewater (Dantas et al., 2007; Deborde, et al., 2008; Yoon et al., 2007; Zhang et al., 2008).

In Malaysia, the research on treatment of EDCs in Malaysia has started to gain some traction. For example, a study done by Razak et al. (2007) on removal of EDCs using nanofiltration system showed that more than 80% of pentachlorophenol (PCP) were successfully removed. Another study by Bolong et al. (2010) demonstrated that more than 90% of BPA is removed using self fabricated nanofiltration membrane. In addition, full degradation of methylparaben was observed under 55 Watts compact fluorescent

lamp using photocatalysis system making this method a good alternative (Lam et al., 2013).

Table 2.3: Physicochemical Treatment of EDCs from various water sources.

Water Matrix	Compound	Treatment Method	Efficiency	Reference
Water	BPA	Ozonation	~100%	Deborde et al. (2008)
	Bezafibrate		~100%	Dantas et al. (2007)
	BPA	Sonochemical Degradation	55%	Pétrier et al. (2010)
	BPA	Ultrasonic	48 - 94%	Gültekin & Ince (2008)
	Various	PAC	14 - 98%	Westerhoff et al. (2005)
	Various	Chlorination	> 90%	
	17β-Estradiol	Membrane Vesicles	82%	Yamamoto et al. (2004)
	PCP	Nanofiltration	> 80%	Razak et al. (2007)
Wastewater	Various	PAC	16 - 95%	Westerhoff et al. (2005)
	Various	Ozonation	6 - 100%	Huber et al. (2003)
	BPA		61%	Snyder et al. (2006)
	BPA	Ultrafiltration	58%	Yoon et al. (2007)
	BPA	Photo - degradation	28%	Neamţu & Frimmel (2006)
	BPA	Nanofiltration	> 90%	Bolong et al. (2009)
Sewage	BPA	Ozonation	100%	Zhang et al. (2008)
	Various		~80%	Nakada et al. (2007)
	Various	O_3 + Sand Filtration	> 80%	
	Various	Anaerobic/ anoxic	> 90%	Nie et al. (2012)
	BPA	Ferro - Sonication	82.7%	Mohapatra et al. (2011)

2.2 Sulphonamide

Based on the data in Table 2.2, sulphonamide is among the highest emerging contaminant (EDCs) detected in Malaysia river basin and the need for sound treatment method is deemed necessary. The following part of the section will discuss the characteristics and occurrence of sulphonamide in the environment together with the current treatment method available to remedy the situation.

In the list of potential EDCs maintained by The Endocrine Disruption Exchange (TEDX), sulphonamide is classified as one of the harmful chemicals that fall under the EDCs group (Colborn, 2012). In general, sulphonamide is a synthetic antibiotic, which is widely used as human medicine to prevent and treat many kinds of bacterial infection. Sulphonamides are also used as veterinary medicine especially in poultry farming for its prophylactic and therapeutic properties which are to increase the rate of growth and prevent illness of livestock.

Uncontrolled use of sulphonamide for the past few years have raised concern due to the fact that these compounds are continuously being introduced into the water bodies (Baran et al., 2011; Gao et al., 2012; Luo et al., 2011). Failing to monitor the uses of sulphonamide especially in healthcare and farming industries would definitely pose an indirect potential threat to human health.

Direct effect of sulphonamide toward human is still inconclusive and requires more studies, however, its effect toward animals are well documented (Schwab et al., 2005). Toxicity study on sulfadimethoxine and sulfamonomethoxine on five aquatic organisms showed that there two compounds are indeed toxic to two species of microalgae (Huang

et al., 2014; Huang et al., 2015). Furthermore, the risk of spreading of bacteria and pathogens that resist the effect of antibiotics are currently the biggest concern regarding the uses of sulphonamide and this issue are in need to be addressed to prevent any undesirable effect to human and environment in the future (Gao, et al., 2012).

2.2.1 Characteristics of sulphonamide

As illustrated in Figure 2.2, sulphonamide functional group (represented in red colour) comprises the sulfonyl group connected to an amide group. At the end of each sides of the sulphonamide functional group are another two groups of moieties. One of the moieties is aniline moiety (represented in blue colour), which is commonly present in all compounds that is under sulphonamide group. Aniline moiety (amino group attached to phenyl ring) is attached via a single bond to S in sulfonyl group.

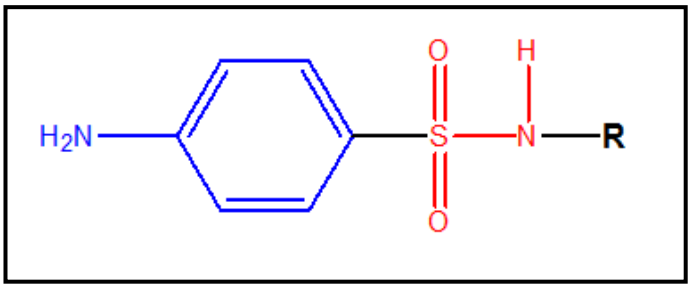


Figure 2.2: Functional group of synthetic antimicrobial sulphonamide
(Source: García-Galán et al., 2008)

The variations of structure found in compounds under sulphonamide group are generally due to the variations of another moiety (**R**) that is connected as a single bond to the N side in sulphonamide amino group. **R** moieties of each type of sulphonamide derivatives are shown in Table 2.4 together with their respective properties.

With acid dissociation constants (pK_a) ranging between 5 and 11, sulphonamide is considered a weak acidic compound but with less acidic properties compared to sulfonic acid, although having similar properties. The difference in functional group between sulfonic acid and sulphonamide is that the hydroxyl group in sulfonic acid is replaced with an amine group in sulphonamide. The lower electronegativity of nitrogen and lower tendency to release hydrogen between these two compounds contribute to the difference in pK_a value between sulphonamide and sulfonic acid.

Table 2.4:**Chemical properties of sulphonamide derivatives**
(Source: Baran et al., 2011)

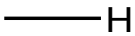
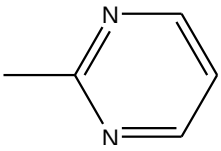
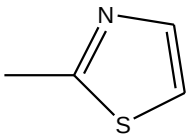
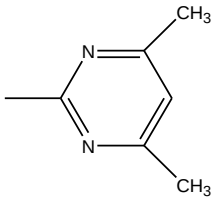
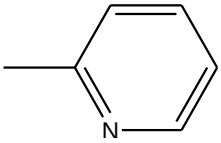
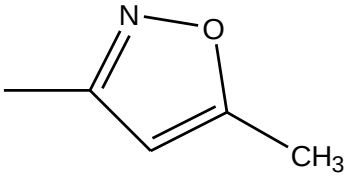
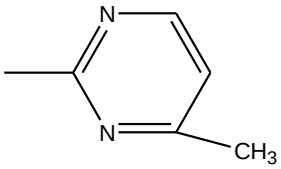
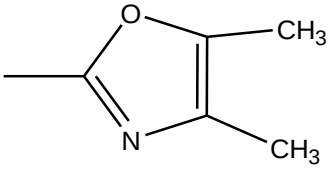
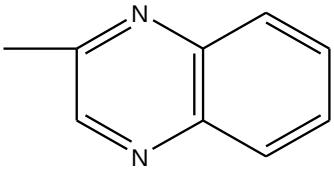
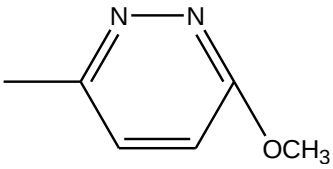
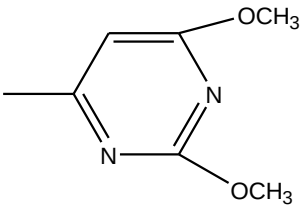
Compound (Abbreviation)	CAS No	Mol. Weight	-R
Sulfanilamide (SAD)	**63-74-1**	**172.2**	
Sulfadiazine (SDZ)	**68-35-9**	**250.3**	
Sulfathiazole (STZ)	**72-14-0**	**255.3**	
Sulfamethazine (SMT)	**57-68-1**	**278.3**	
Sulfapyridine (SPY)	**144-83-2**	**249.3**	

Table 2.4: continued

Compound (Abbreviation)	CAS No	Mol. Weight	-R
Sulfamethoxazole (SMX)	**723-46-6**	**253.3**	
Sulfamerazine (SMR)	**127-79-7**	**322.4**	
Sulfamoxole (SMM)	**729-99-7**	**267.3**	
Sulfaquinoxaline (SQX)	**59-40-5**	**300.3**	
Sulfamethoxipyridazine (SMPD)	**80-35-3**	**280.3**	
Sulfadimethoxine (SDM)	**122-11-2**	**310.3**	

Previous study by Dodd & Huang (2004) showed that sulphonamide exhibit two pK_a values, in which both are depends on the specific pH condition of the compound . One of the pK_a values was derived from a deprotonation of acidic amide group at pH 4.5 – 11 by releasing a proton in

NH bond while the other pK_a value was obtained from a protonation of basic amine group at pH 2 – 3 by gaining a proton into aniline N. The dissociation equilibrium of sulphonamide showing anionic, neutral and cationic forms is shown in Figure 2.3.

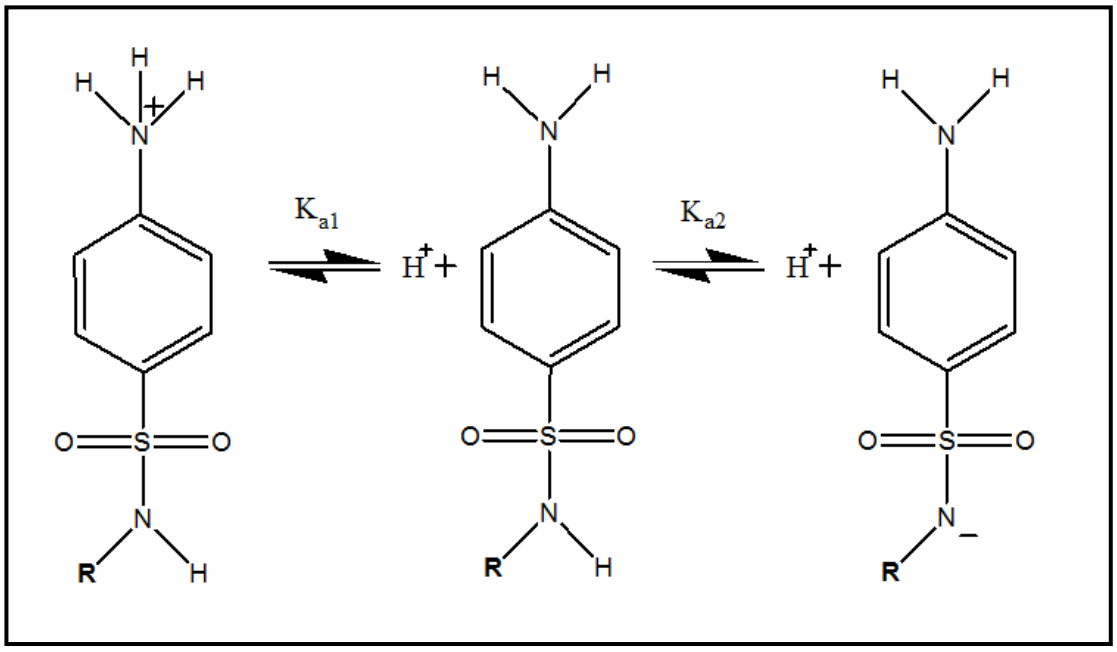


Figure 2.3: **Speciation of sulphonamide**
(Source: Qiang & Adams, 2004a)

2.2.2 Uses of sulphonamide

Sulphonamide is a well known antibiotic that was used to treat bacteria-induced diseases in human such as inflammatory bowel disease, urinary tract infection, and pneumonia. Now sulphonamide is mostly used in veterinary applications as therapeutic (to promote the growth of livestock) and also as medicine (to treat livestock). Among many sulphonamide derivatives, sulfamethoxazole and sulfasalazine are generally used as human medicine while sulfamethazine, sulfadiazine, sulfadimethoxine and sulfathiazole are mainly used for veterinary purposes (Baran, et al., 2011).

In Malaysia, the data on the usage of sulphonamide is very limited. One analysis by Cheong et al. (2010) on sulphonamide usage in chicken meat products around peninsular Malaysia estimated that between 24.77 and 32.77 g/day of sulphonamide were consumed by chicken which leaves an unmetabolized sulphonamide in chicken meat up to 0.152 µg/g, which is higher than the residue limit set by European Union Regulation (1990). A monitoring on sulphonamide concentration in three states river (Perak, Melaka, and Selangor) near swine poultry wastewater effluent found that 103 out of 300 samples collected were found positive for sulphonamide with concentrations between 5 ng/L to 95 ng/L were detected (Malintan & Mohd, 2006).

Although the use of sulphonamide in Malaysia is currently not restricted, other countries such as Europe have set regulations and restrictions on the use of sulphonamide especially in animal husbandry (European Union Regulation, 1990). The use of sulphonamide for the purpose of promoting the growth rate of livestock in animal poultry has been prohibited by the European Union beginning in 2006 (Sarmah et al., 2006). However, the use of sulphonamide in animal husbandry and medicine nowadays does not seem to decrease much compared to before the restriction was introduced (Baran, et al., 2011).

2.2.3 Occurrences of sulphonamide in the Environment

Studies on the occurrence of sulphonamide in the environment have been conducted extensively for the past years (Gao, et al., 2012; Hoa et al., 2011; Murata et al., 2011; Wei et al., 2011). Limited quantitative data about sulphonamide found in river water was first published in the year 1984 (Sarmah, et al., 2006). Since then, the quantification of sulphonamide became much easier and more accurate due to the development of

more advanced analytical instruments such as liquid chromatography-mass spectrometry (LC-MS/MS) and solid phase extraction (SPE).

Sulphonamide can enter the environment through many pathways. It can be from industrial effluents, improper waste management and leaching from livestock manure into soil. A number of sulphonamides have been detected in the environment especially in wastewater effluent and surface water. The concentration of sulphonamide found in different type of water matrix is summarized in Table 2.5.

In Table 2.5, the highest concentrations of sulphonamide were found in animal wastewater resulting from the leaching of manure or wastewater that contained unmetabolized or residues from sulphonamide given to livestock in nearby animal husbandry. Unmetabolized sulphonamide excreted from human bodies also contributed to the high concentration of sulphonamide found in hospital wastewater effluent and also in surface water. (Lin & Tsai, 2009; Murata, et al., 2011). Another study by Schwab et al. (2005) shows a concentration as high as 8.5 µg/L and 18 µg/L of sulfamethoxazole in drinking water and surface water, respectively. On the other hand, unwanted drugs or medicines that ended up in landfill also contributed to the presence of sulphonamide in the environment (Schwab, et al., 2005).

In Malaysia, detection of sulphonamide in river water was done by a team of researchers from University of Malaya (Malintan & Mohd, 2006). The samples were collected from three states (Perak, Malacca, and Selangor) in two replicates where in each replicate a total number of 100 samples were collected for each state. Out of 300 samples collected, 103 were found positive for sulphonamide. From the results obtained, sulphonamide was detected in all three states with a range of concentration

between 5 ng/L to 95 ng/L in which sulfanilamide and sulfadiazine gave the highest concentration and the most frequent compound detected.

Table 2.5: **Concentration of sulphonamide found in environment**

Water Matrix	Compound	Concentration Detected (µg/L)	References
Wastewater Influent	SMX	0.05 - 1340	Lin & Tsai (2009)
	SMT	0.0269 - 500	Babić et al. (2006)
	STZ	1158.68	Choi et al. (2007)
Wastewater Effluent	SMX	0.00366 - 6.0	Batt et al. (2006)
	STZ	0.005 - 4.27	Choi et al. (2007)
Hospital Wastewater	SMX	12.8	Lindberg et al. (2004)
	Various	92.8	Kümmerer & Henninger (2003)
Animal Wastewater	SMT	211	Wei et al. (2011)
	SDZ	17	
Seawater	SMX	0.0475	Minh et al. (2009)
Surface Water	SMX	0.015 - 18	Schwab et al. (2005)
	SMT	0.0108 - 19.2	Managaki et al. (2007)
	Various	> 25	Díaz-Cruz et al. (2008)
	Various	0.0024 - 0.385	Luo et al. (2011)
	Various	0.626	Murata et al. (2011)
	Various	< 0.09495	Malintan & Mohd (2006)
Ground Water	SMX	0.0099 - 1.11	Barnes et al. (2008)
	SDM	0.09148	García-Galán et al. (2010)
	SCT[a]	3.461	
Bottled Mineral Water	SDM	0.000164	Perret et al. (2006)
	SMX	0.080	
Drinking Water	SMX	8.5	Schwab et al. (2005)
	STZ	0.011	
Leachate	SCP[b]	0.66 - 703.2	Kay et al. (2005)

[a] SCT = sulfacetamide, [b] SCP = sulfachloropyridazine

Currently, concentration of sulphonamide detected in the environment is still at a trace level (ng/L) which is way lower that the concentration to be considered dangerous to human health (mg/L level) (Baran et al., 2006). However, sulphonamides are shown to have a high resistivity towards degradation in water and as a result, its concentration will likely to increase to a dangerous level in the near future (Pérez et al., 2005). A study conducted by Perez et al. (2005) on the biodegradability of three sulphonamide in surface water shows no noticeable degradation even after more than a month . This phenomenon suggests the importance of elimination of sulphonamide from water bodies.

2.2.4 Previous Studies on Removal of sulphonamide

2.2.4.1 Conventional Wastewater treatment plant

Various studies conducted on the removal of antibiotics using conventional wastewater treatment plants shows that the removal of sulphonamides are incomplete due to limited degradability (Behera et al., 2011; Ghosh et al., 2009; Xu et al., 2007). The concentration of sulphonamide detected in influent and effluent of different wastewater treatment plants as published by several researches are shown in Table 2.6

Sulphonamide removal efficiency appears to be connected to the types of treatment employed in wastewater treatment plants. Wastewater treatment plant using a combination of activated sludge and ultraviolet (UV) showed higher rejection rate compared to the plant that using activated sludge only (Chang et al., 2008; Ghosh, et al., 2009). In some cases of wastewater treatment plants, concentration of sulphonamide detected in effluent was higher compared to the influent. For example, the wastewater treatment plant in Switzerland showed higher concentration of sulfamethoxazole detected in effluent compared to the influent (Göbel et al., 2007; Li et al., 2009; Yang et

al., 2005). This effect is due to retransformation of the main human metabolite of sulphonamide, N^4-acetylsulphonamide which is present in the wastewater that can be traced back to its parent compound by means of hydrolysis (García-Galán et al., 2008). Another study done by Dodd & Huang (2004) showed that the chlorine molecule that attached to the sulphonamide formed N-chlorinated will retransform to the parent compound by releasing the chlorine molecule in the absence of chlorine agent and thus increases the concentration of sulphonamide in the effluent.

Table 2.6: **Sulphonamide removal efficiencies in Wastewater treatment plant**

Country	Treatment Method	Comp	Influent (ng/L)	Effluent (ng/L)	Reference
China	AS and Cl_2	SMX	16	16	Xu et al. (2007)
Korea	AS	STZ	30 - 531	< 30	Choi et al. (2008)
		SDM	10 - 213	< 10 - 70	
		SCP[b]	30 - 476	< 30 - 149	
USA	AS and Cl_2	SMX	1090	210	Yang et al. (2005)
	AS	SMX	80 - 1250	50 - 210	Karthikeyan & Meyer (2006)
		SCT[a]	70	0	
Switzerland	AS and SF	SMX	230 - 570	211 - 860	Göbel et al. (2007)
		SPY	60 - 150	40 - 350	
Japan	AS	SMX	6.9 - 27	24 - 28	Chang et al. (2008)
	AS and Cl_2	SMX	180	133	Ghosh et al. (2009)
		SDT	70	26	
Hong Kong	AS and DN	SMX	10	12	Xu et al. (2007)
	PT	SMX	-	31.8 - 278	Minh et al. (2009)
	-	SDZ	73	20	Li et al. (2009)
Canada	PT, AS, Cl_2, UV and TF	SMX	-	243 - 871	Miao et al. (2004)
		SPY		81 - 228	
		SDZ		19	

AS = Activated Sludge, Cl_2 = Chlorination, UV = UV disinfection, F = Filtration, PT = Primary Treatment, DN = denitrification, TF = Trickling Filters, CAS = conventional activated sludge

2.2.4.2 Advanced Treatment

Over the last few years, several new techniques have been explored for sulphonamide removal from water bodies. Due to the low removal efficiencies of conventional water and wastewater treatment plants, new and more advanced treatment is required to produce better quality effluent. The removal efficiencies of sulphonamide compound from water and wastewater by various physiochemical treatment methods is summarized in Table 2.7.

From the compiled data, it was revealed that high removal efficiency was achieved by using a variety of treatment methods such as oxidation and advanced oxidation process (ozone, chlorine), photocatalytic process, and fenton and photo-fenton processes. Although having high removal efficiency, these treatment methods are relatively costly compared to conventional treatment system (Esplugas, et al., 2007). Moreover, higher concentration of organic pollutant present in the influent resulted in more chemicals/agents required for effective elimination. This will further increase the operating cost.

Not only that, some of the method produces intermediates and final by-products that are higher in toxicity compared to its original compound (Chamberlain & Adams, 2006; Dantas et al., 2008). Acute toxicity test on by-product formed during ozonation process of sulphonamide showed that sulfamethoxazole (SMX) intermediate by-product formed in the first 30 minutes has higher toxicity compared to untreated SMX (Dantas, et al., 2008). The toxicity values then reduce closer to the original value after 30 minutes.

The combination of two or more treatment system (e.g. Ozone/H_2O_2 or UV/H_2O_2) gave better rejection rate compared to single treatment method (Lin, et al., 2009). However, operational cost for combined system would definitely be higher compared to single treatment. The combination or hybrid treatment system is only suitable if high quality treated water is required (e.g. ultrapure water or drinking water).

Table 2.7: **Physicochemical Treatment of sulphonamide**

Water Matrix	Treatment Method	SNs	Efficiency / Rate of Degradation	Reference
Pure / Surface Water	AOPs Ferrate	SMX	91 - 241s	Sharma et al. (2006)
	Hypochlorite		6 - 181s	
	Ozone		< 99% after 60min	Dantas et al. (2008)
	Reverse Osmosis		< 99%	Radjenović et al. (2008)
	Nanofiltration		~ 60%	Koyuncu et al. (2008)
	TiO_2		~ 88%	Baran et al. (2006)
		SAD	~ 50% after 20 min	Baran et al. (2009)
	TiO_2 / $FeCl_3$		< 90% after 90min	
	Photo Fenton	Mixture	< 100%	González et al. (2007)
	Fenton		> 90%	Ben et al. (2009)
	Ozone / H_2O_2		< 99%	Lin et al. (2009)
	UV / H_2O_2		> 90%	Kim et al. (2009)
	Chlorine		< 88%, k =0.00025-0.00347s^{-1}	Chamberlain & Adams (2006)
	Ionic Treatment		> 90%	
Waste Water	MIEX® Resin		40 - 90%	Choi et al. (2007)
	TiO_2		15 - 30% after 1hour	Justyna et al. (2010)
	TiO_2 / $FeCl_3$		62% - 84%	
	Coagulation		0 - 21.3%	Suarez et al. (2009)
	Bacterial Degradation	SMX	0 - 15%	Larcher & Yargeau (2011)

2.3 Membrane Filtration

From on the data collected in Table 2.7, membrane filtration technology such as reverse osmosis and nanofiltration has shown that these treatment methods are noteworthy for the rejection of EDCs, thus nanofiltration membrane was chosen as membrane process for the removal of sulphonamide in this study. The following part of the section will discuss the mechanism of the membrane filtration particularly nanofiltration system in removing EDCs especially sulphonamide.

2.3.1 Mechanisms of Membrane Filtration

A membrane is a thin layer of semi permeable material that operate as a selective barrier in separating the mixture of compound by rejecting certain compounds while allowing the other compounds to pass through. Since membranes are very thin (around 0.1mm to 0.5mm in thickness), they are usually mounted on a thick supportive matrix in order to increase their stability (Pendergast & Hoek, 2011).

There are three main separation mechanisms in membrane filtration, which are:

i) Size exclusion (sieving), where the difference between MWCO of the membrane and molecular weight of particles determines the rejection efficiencies (Derjani-Bayeh & Rodgers, 2002). Particles with larger molecular size than the membrane pore size will mostly be rejected by the sieving mechanism.

ii) Charge repulsion, where the interactions between the membranes surface charges and the particles with different electronegativity occur (Kallioinen & Nyström, 2008). In

this mechanism, the pH of the solution plays an important part in determining the charge of the solute and also changes on the membrane surface. Particles with the same polarity as the surface of the membrane will likely be repelled by the membrane, and thus increased the rejection efficiencies.

ii) Adsorption, where the particles will adsorb onto the membrane surface due to psysico-chemical interaction between them. (Comerton et al., 2007). The extent of adsorption greatly depends on the ionic strength of the solution and membrane materials. Membranes with hydrophilic material are less susceptible to adsorption compared to the membrane with hydrophobic material (Mulder, 2003).

Figure 2.4 illustrate the flow of membrane rejection mechanism. Transmembrane pressure (TMP) is the driving force that makes the filtration process possible. TMP is the difference in pressure between feed side and the permeate side. With the help of pressure (driving force), certain compound contained in the feed will be rejected (retained) by the membrane while the rest will passed through into the membrane. Compounds that passed through the membrane are called permeate or filtrate while the rest of the rejected compounds are called retentate.

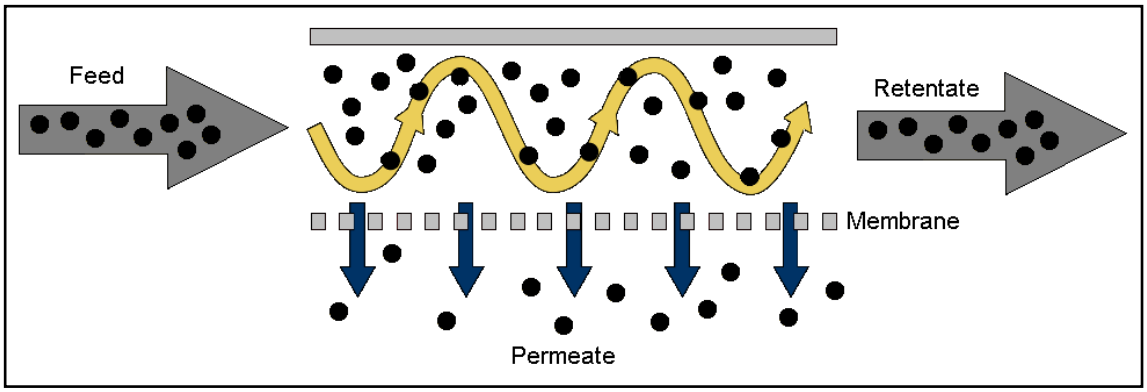


Figure 2.4: **Membrane rejection mechanism**

2.3.2 Type of Membranes

There are various types of membrane material currently available for membrane fabrication. Membrane can be manufactured using either inorganic membrane material such as ceramic, zeolite, glass and oxide or organic membrane material such as cellulose acetate, nylon, polyethersulfone and polyamide (Pendergast & Hoek, 2011; Uemura & Henmi, 2008). Among these materials, inorganic material such as ceramic is among the best material for membrane manufacturing because of their inert reaction with chemical and able to withstand high operating pressure and temperature compared to their polymeric counterpart (Padaki et al., 2015). However, polymeric material such as polyamide is a more compatible material for nanofiltration and reverse osmosis membrane in water and wastewater treatment plants due to its significant low cost production compared to other types of materials (Van der Bruggen & Geens, 2008).

There are also various types of membrane classification with different pore size such as reverse osmosis, nanofiltration, ultrafiltration, and microfiltration (Côté et al., 2008). The differences in pore sizes between each membrane type are clear. Molecular size of particles or compound that need to be separate will determine which membrane type is suitable. Microfiltration with the largest pore size compared to the other membrane is usually used to concentrate fine colloidal suspension and separate suspended solids. Since nanofiltration membrane has a smaller pore size compared to ultrafiltration membrane, nanofiltration can reject both monovalent and multivalent ions while ultrafiltration can only reject multivalent ions.

Being a less pore membrane, reverse osmosis membrane can rejects almost anything while only allowing solvent like water to pass freely through the membrane. This

membrane is suitable for producing very high quality potable water. Figure 2.5 portrays the types of particles or solutes that can be rejected by different types of membrane.

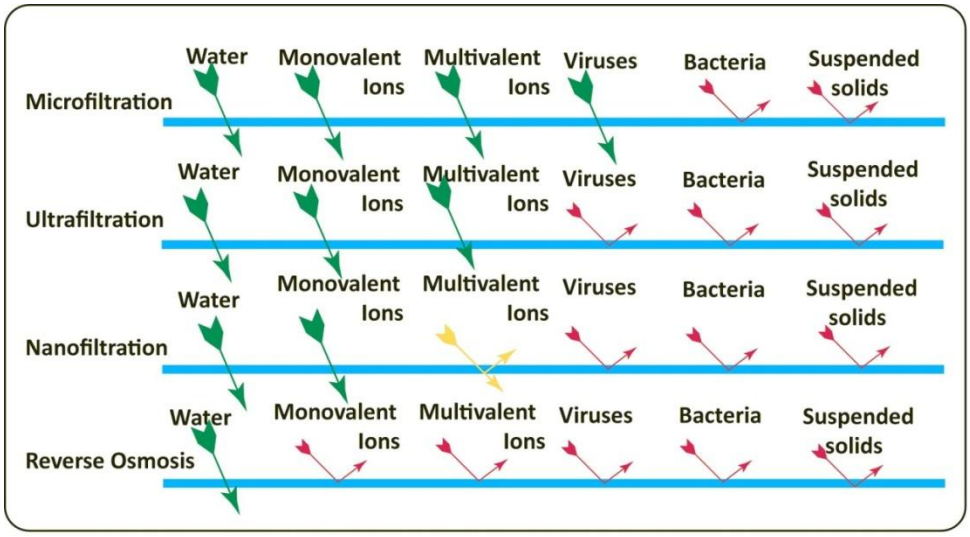


Figure 2.5: Membrane filtration spectrum shows the ability of all membrane to selectively reject certain types of particles.
(Source: TRISEP Corporation (2012))

Apart from experimental results, a rough estimation of rejection capabilities based on the physicochemical properties of the targeted compound can also be predicted. In particular, prediction on rejection of pesticides that takes into account the properties of solute retention trends (membrane, foulant and solute) was summarized by Plakas & Karabelas (2012) and showed in Figure 2.6 and Figure 2.7. In both diagram, the trend in rejection of pesticide by nanofiltration is highly dependent on the differences between molecular weight of pesticide and molecular weight cut off of membrane. High rejection of pesticide can be achieved when molecular size of pesticide is bigger than the membrane molecular weight cut off. Coefficients of octanol-water ($\log K_{ow}$) together with the hydrophobicity of natural organic matter (NOM) present also contribute to the efficiencies of pesticide removal.

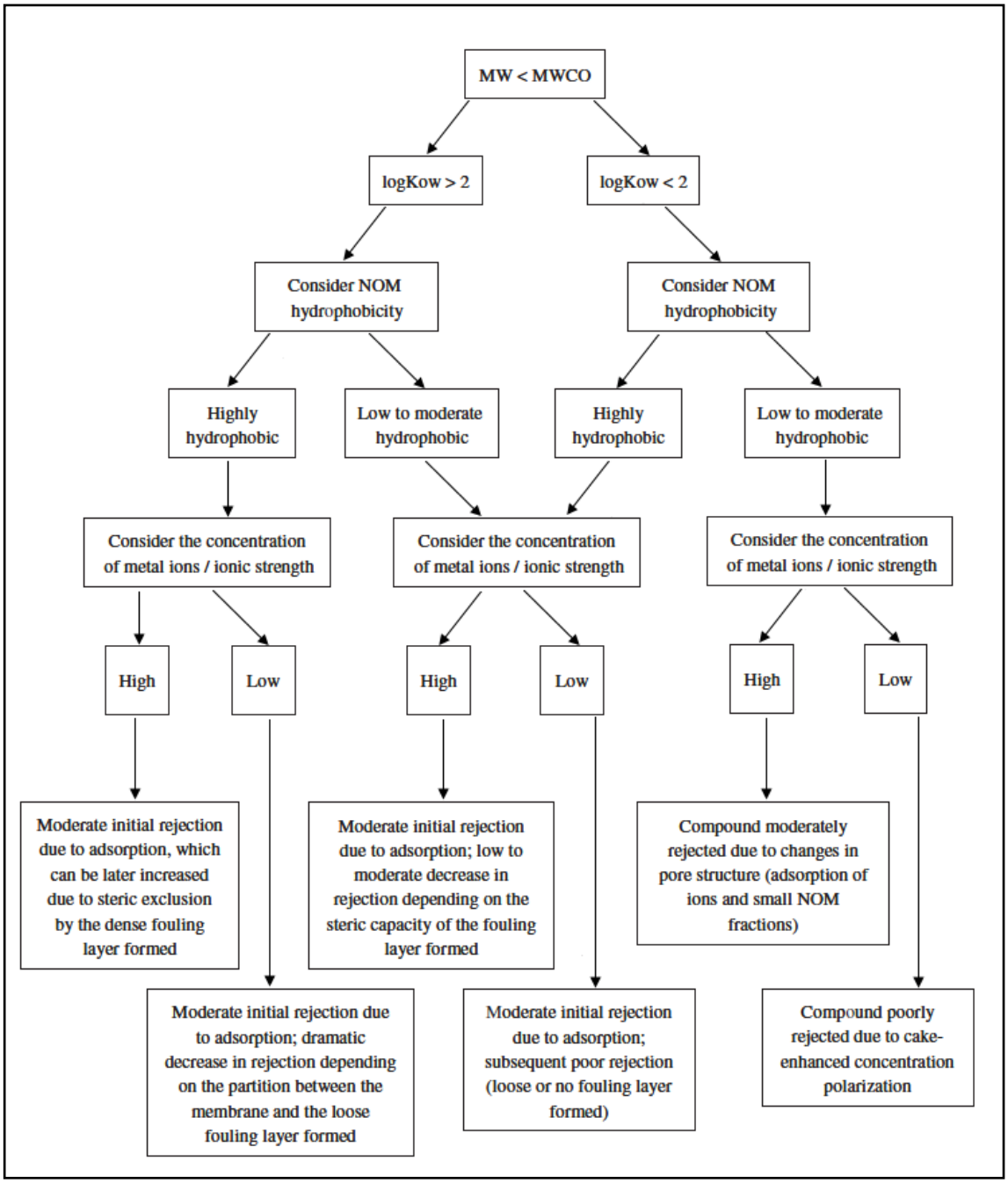


Figure 2.6: **A diagram on the guidance regarding the solute retention trend in rejection of pesticides (with molecular weight *smaller* than membrane WMCO) in water using nanofiltration membrane.**
(Source: Plakas & Karabelas, 2012)

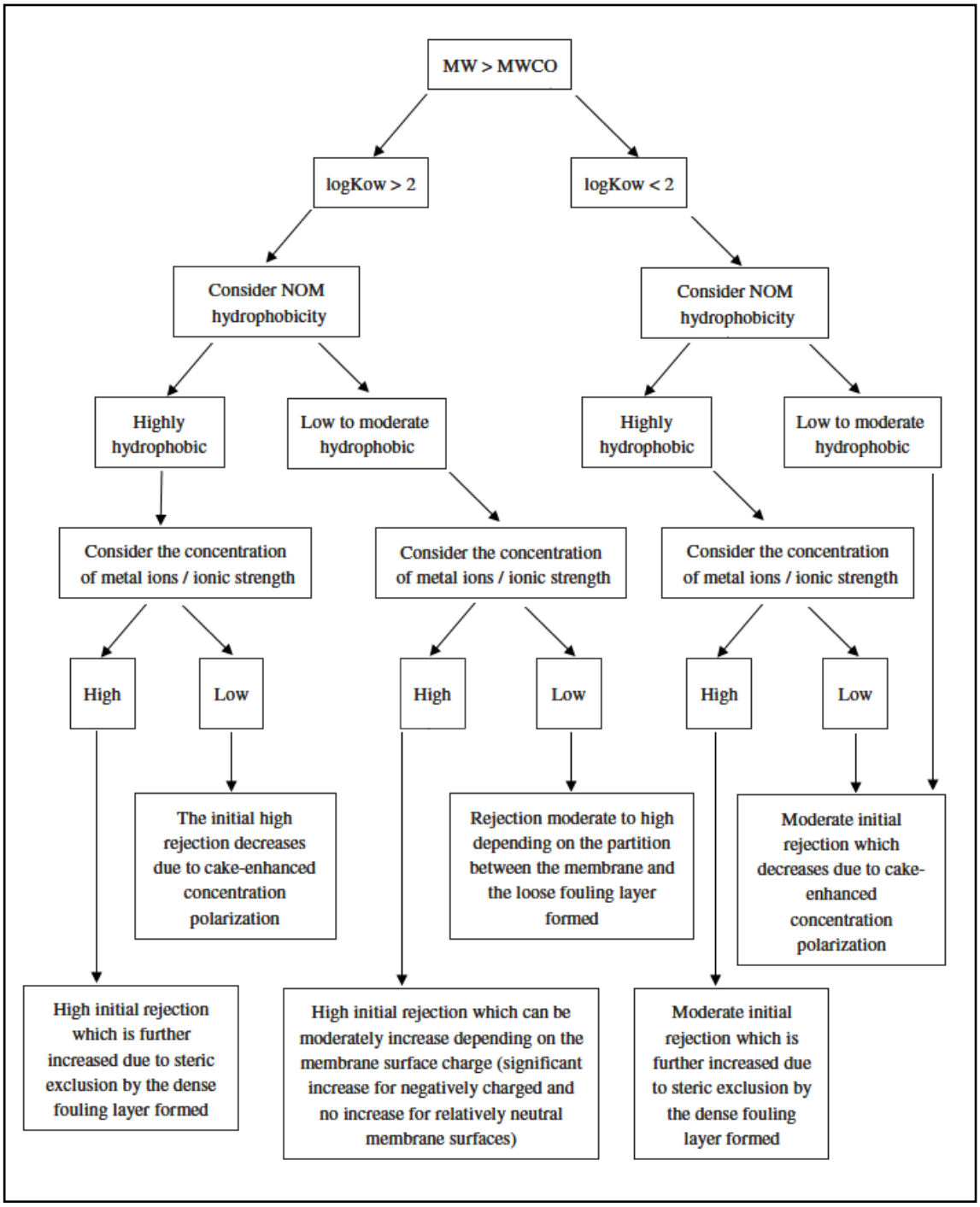


Figure 2.7: **A diagram on the guidance regarding the solute retention trend in rejection of pesticides (with molecular weight *bigger* than membrane WMCO) in water using nanofiltration membrane.**
(Source: Plakas & Karabelas, 2012)

2.3.3 Nanofiltration

In 1970, nanofiltration membrane was developed, with the aim of producing a reasonable water flux at low pressure but with the effluent characteristic that is as good as reverse osmosis membrane (Zhang et al., 2012).

Nanofiltration is the second in line to possess smallest pores in membrane after reverse osmosis membrane. Having known as low pressure reverse osmosis membrane, nanofiltration membrane has almost all the properties of reverse osmosis membrane but with the ability to operate efficiently at much lower pressure.

Based on the rejection performance, nanofiltration membrane is divided into two types, loose nanofiltration and tight nanofiltration. The differences between these two nanofiltration membranes are mainly on rejection efficiencies together with water flux resulted from the differences in MWCO (Van der Bruggen & Geens, 2008).

Tight nanofiltration, with MWCO ~200 Dalton has a higher salt rejection rate but lower pure water permeability while loose nanofiltration with MWCO ~300 Dalton have a higher pure water permeability even though showing lower rejection rate. Required quality level of effluent will determine which types of nanofiltration membrane are suitable to be used in the filtration process (Xu et al., 2005).

2.3.3.1 Previous Studies on Removal of EDCs by Nanofiltration

Conventional water and wastewater treatment plants were designed for the purpose of producing tolerable level of water effluent set by existing regulation. Yet, the occurrence of non-existence regulation for emerging micropollutants such as EDCs and PPPCs and PhACs in water and wastewater effluent has become a problem. Over the past years, considerable amount of research effort has been devoted in developing a better treatment method to effectively remove these kinds of micropollutants.

Advance separation processes such as ion exchange, membrane filtration and adsorption shows promising results in removal rate (Delgado et al., 2012; Esplugas, et al., 2007). By taking into account that most of the micropollutant have molecular size around 1 nm (above 150Da), a pressure driven membrane process especially nanofiltration is efficient in removing these micropollutants. The summary on removal of micropollutant (EDCs, PPCPs and PhACs) in different types of water matrix by nanofiltration membrane is shown in Table 2.8. Although nanofiltration requires a higher operating pressure, nanofiltration membrane with smaller molecular weight cut-off (tight membrane) such as NF90 shows a better rejection rate compared to another type of membrane that have a larger MWCO than NF90. In addition, 91.5% of Bisphenol A (BPA) were removed from water using NF90 membrane (Yangali-Quintanilla et al., 2009) while more than 99% of chlorpyrifos were removed by NF270 nanofiltration membrane in surface water (Kiso et al., 2000). Moreover, 99.4% of sulfadiazine was observed to be removed using NF90 membrane in simulated wastewater (Košutić et al., 2007).

Table 2.8: **Percentage of micropollutant removed during treatment from different types of water matrix using commercial nanofiltration membrane.**

Type of Water	Membrane Model	Compound	Mol. Wt.	Rejection (%)	Reference
Pure Water	NF270	Estrone	270	65 ± 3	Braeken & Van der Bruggen (2009)
		Estradiol	272	85 ± 4	
		Salicine	286	91 ± 1	
		Caffeine	194	12 ± 0.7	Comerton et al. (2008)
	TS80	17α-Estradiol	272	46 ± 9.3	
		Acetaminophen	151	29 ± 2.5	Comerton et al. (2009)
		Oxybenzone	228	5 ± 2.3	
		Carbamezepine	236	93 ± 0.8	
	NF90	Bisphenol A	228	91.5	Yangali-Quintanilla et al. (2009)
		SMX	253	94.5	
		17β-Estradiol	272	92.7	
		Nonylphenol	220	91.3	
		Sulfadiazine	251	99.4	Košutić et al. (2007)
Surface	TS80	Bisphenol A	228	71 ± 9.7	Comerton et al. (2009)
		17α-Estradiol	272	81 ± 7.2	
		17β-Estradiol	272	78 ± 8.8	
	NF270	Ibuprofen	206	30 - 95	Bellona & Drewes (2005)
		Simazine	202	88 - 93	Chen et al. (2004)
		Progesterone	314	90 - 100	Nghiem et al. (2004)
		Testosterone	288	80 - 100	

2.4 Chlorination

Although membrane technology especially nanofiltration (NF) and reverse osmosis (RO) are being used widely to treat micropollutant (Snyder et al., 2007), the practices of direct filtration using these membranes are limited due to membrane fouling (Comerton, et al., 2009; Verlicchi, et al., 2009). Furthermore, separation method is mainly being a

physical treatment, therefore the filtration process does not actually eliminate the accumulated retentate and disposal of retentate would be required (Van der Bruggen, et al., 2008). To counter these problems, a membrane pre-treatment process is required in order to help reduce the fouling and to transform or eliminate the accumulated retentate.

Chlorination is proven to be an excellent pre-treatment and disinfection method by reducing the compound that are likely to induce membrane fouling such as suspended solid, biodegradable organics and nutrients in the feed (Friedler et al., 2008; Üstün et al., 2011). Chlorine can also helped by partially cleaning the surface of the fouled membrane (Kang, et al., 2007). However during chlorination, a residual natural organic matter (NOM) that are still present in wastewater may react with available chlorine and as a result a carcinogenic disinfectant by-product (DBPs) such as trihalomethanes (THM) and haloacetic acid (HAA) were produced (Deborde & von Gunten, 2008; Shen & Andrews, 2011). Although these dangerous by-product were formed during pre-treatment, nanofiltration membrane were able to effectively removed NOM and its by-product produced from the pre-treatment effluent (Ates, et al., 2009; Doederer et al., 2014; Zularisam et al., 2006).

2.4.1 Chlorine Speciation

According to (Deborde & von Gunten, 2008), chlorine may exist as hypochlorite ion (ClO^-) or as hypochlorous acid (HOCl), depending on the pH of the solution. Hypochlorous acid (HOCl) exists as dominant species in the acidic region while hypochlorite ion (ClO^-) in the basic region with pH 7.5 acting as equilibrium between these two species. The fraction of both chlorine species as a function of pH could be calculated from the Equation 2.1 (Deborde & von Gunten, 2008):

$$\alpha OCl^{-} = [1 + (10^{-7.5} \times 10^{pH})]^{-1} \quad \text{-Eq (2.1)}$$

where αOCl^- is the fraction of free chlorine in hypochlorite form and $\alpha HOCl$ is the fraction of free chlorine in hypochlorous acid form.

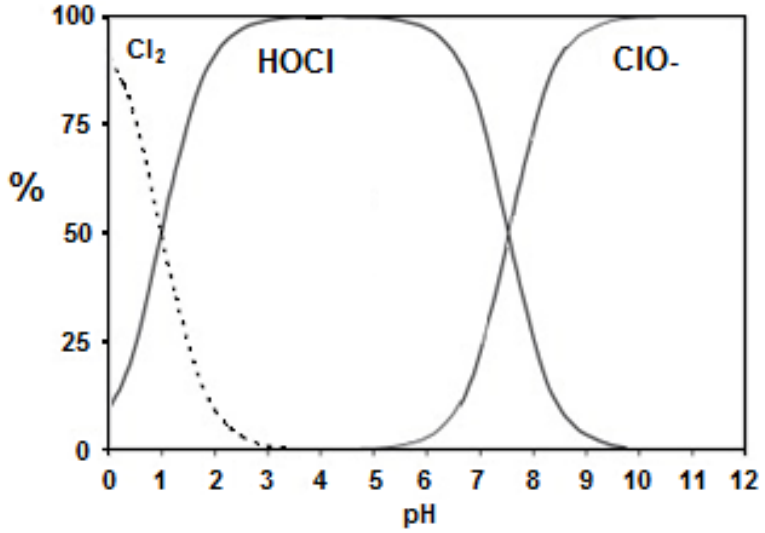


Figure 2.8: **Fraction of chlorine species as a function of pH at 25°C**
(Source: Deborde & von Gunten, 2008)

The relative distribution of chlorine species at various ranges of pH is as shown in Figure 2.8. The reactivity of chlorine is highly dependent on the fraction of chlorine species present in the solution. Based on a few study on reaction of chlorine with organic compound, chlorine were found to be more reactive in acidic region where HOCl is dominant compared to the basic region where OCl^- is dominant. In this study a wide range of pH covering acidic and basic region will be conducted in order to monitor the effect of various combination of chlorine species to the removal of sulphonamide.

2.5 Summary of Current Literature Review

Disinfection process is a must for every water treatment plants and for certain wastewater treatment plants (Schilirò et al., 2009; Verlicchi, et al., 2009). The purpose of disinfection is to kill off the dangerous pathogens including untreated organics from the upstream part of the treatment process.

However, various studies conducted on the removal of endocrine disrupting compounds (EDCs) and pharmaceutically active compounds (PhACs) showed incomplete removal, which is mainly due to the limited degradability of these micropollutants, combined with low molecular size of micropollutants (Huerta-Fontela, et al., 2011; Rivera-Utrilla, et al., 2013). As a result, an increased number of organic micropollutants such as EDCs that are present in the effluent had rendered the disinfection process in the treatment plants ineffective (Chen et al. 2008). This creates a secondary problem such as formation of dangerous disinfection by-products and may cause repercussion on treated water.

Studies showed that nanofiltration and reverse osmosis have the ability to remove low molecular weight organic contaminants, including the disinfection by-products (Koyuncu et al. 2008; Al-Rifai et al. 2011; Dolar et al. 2011). However, membrane processes are unable to destroy organic pollutants, and as a result of this, rejected pollutants will accumulate in the retentate. Chlorine, with the capability to degrade organic pollutants can be considered a good pre-treatment prior to the membrane process.

Research on application of chlorine or any other oxidation agents prior to membrane process are scarce. This is due to the weakness of organic membrane towards oxidation process. However, with proper control of the membrane operating condition may contribute to the increase of the membrane performance and lifetime. One study conducted by Zhai et al. (2011) even showed that controlled hypochlorite treatment could actually improve the membrane performance in terms of permeate flux, NaCl rejection and also Boron removal.

CHAPTER 3

RESEARCH METHODOLOGY

The study on the removal of sulphonamide consisted of two main objectives as shown in Figure 3.1. The objectives were divided into two parts of experiments which were kinetic behavior during chlorination of sulphonamide and performance of hybrid system which combines chlorination and nanofiltration processes. The process started with the process of literature review collection. Next are the sample preparation processes where the process of preparing sulphonamide working solution and sodium hypochlorite as free active chlorine (FAC) for later uses. Results collected in both studies will be analyzed and then convert into presentable results.

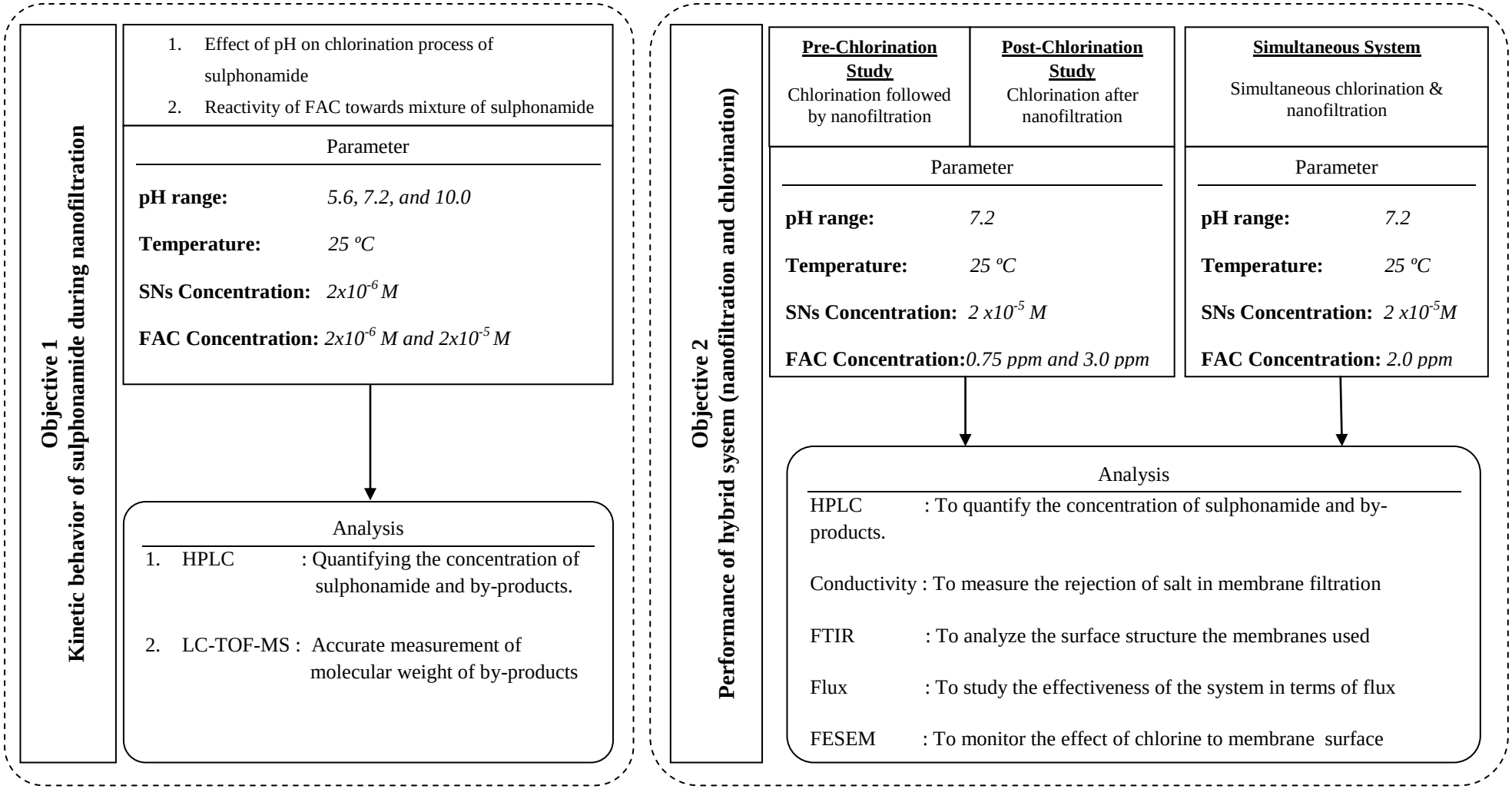


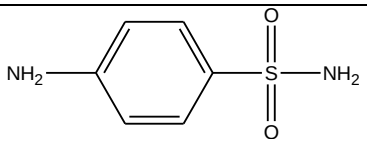
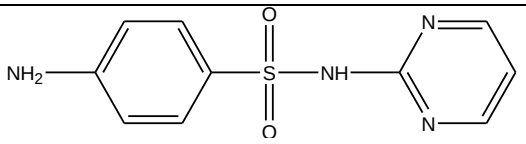
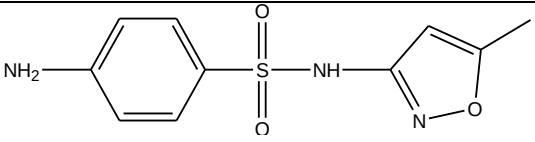
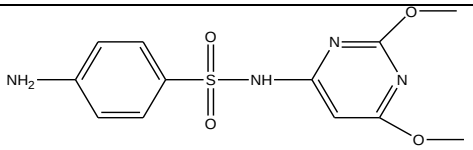
Figure 3.1: Flow Chart of Research Methodology

3.1 Sample Preparation

3.1.1 Materials

A high purity (≥99 %) of sulphonamide derivatives (sulfanilamide [SNM], sulfadiazine [SDZ], sulfamethoxazole [SMX], and sulfadimethoxine [SDM]), sodium hypochlorite, tris (hydroxymethyl) aminomethane (THAM) and sodium sulfite were obtained from Sigma Aldrich (MO, USA). Methanol, acetonitrile, sodium hydroxide, ammonium chloride and hydrochloric acid, acetic acid, and phosphate buffer however, were obtained from Merck (MJ, USA). All of the chemical purchased were used directly without any purification. The physicochemical properties of all four sulphonamide used are compiled in Table 3.1.

Table 3.1: **Chemical Properties of sulphonamide Derivative**

Name (CAS No.)	M.W.	pK_a (a)	Molecular Structure
Sulfanilamide(SNM) (63-74-1)	172.2	10.1	
Sulfadiazine(SDZ) (68-35-9)	250.2	6.50	
Sulfamethoxazole(SMX) (723-46-6)	253.2	5.90	
Sulfadimethoxine(SDM) (122-11-2)	310.3	6.30	

(a) Sethuraman, 2008

In this study, four derivatives were chosen to represent sulphonamide antibiotics because of their high occurrence in Malaysian environment (Malintan & Mohd, 2006).

3.1.2 Membrane Unit

3.1.2.1 Membrane

A flat sheet of aromatic polyamide composite nanofiltration membrane (4040-TS80-TSF) manufactured by TRISEP Corporation (CA, US) was employed in this experiment. Aromatic polyamide composite material is a commonly used polymeric material for nanofiltration membrane due to its good rejection capabilities compared to other types of polymeric materials (Van der Bruggen & Geens, 2008). This membrane was made with three different layers where each layer consists of different material and function. The bottom layer which acted as support sheet was made from 0.1 mm thick of non-woven polyester film and the middle layer consists of a thin layer (0.05 mm thick) of polysulfone ultrafiltration membrane. The top membrane which is 0.2 µm thick was made polyamide and coated into the other layer together. Figure 3.2 shows the overall layers of a polyamide composite membrane.

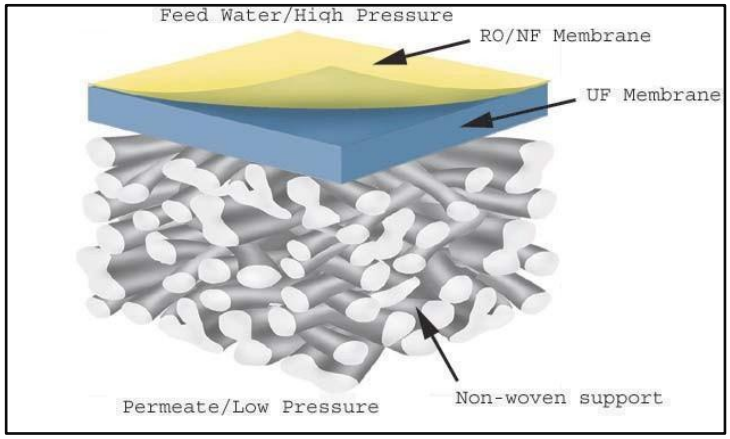


Figure 3.2: Thin Film Polyamide Composite Membrane
(Adopted from TRISEP Corporation (2012))

Based on the specification given by the manufacturer, when tested with 2,000 ppm of $MgSO_4$ solution at 7.5 bar pressure in 30 minutes of operation, a range of 97% to 99% salt rejection was achieved. Proposed molecular weight cut-off (MWCO) for the

membrane as given by the manufacturer is 200 Dalton. The purchased membrane was cut down to smaller sheet with a dimension of 7.5 cm x 15 cm. The effective area (MEA) of the membrane was calculated and determined to be at 40.92 cm^2.

3.1.2.2 Nanofiltration system

Nanofiltration process was conducted throughout the entire experiment using a SOLTEQ-TR32 Benchscale Nanofiltration System developed by Solution Engineering Holdings Berhad (KL, Malaysia). This cross-flow nanofiltration system consists of two units of 1.5 L reservoir to store working solution, metering pump, and two different types of interchangeable membrane modules which are tubular membrane module and flat sheet membrane module. Since thin film nanofiltration membrane was employed for these experiments, a flat sheet membrane module was chosen as the mode of nanofiltration process. Pressure gauges are placed before and after the membrane modules to study the pressure drop when the feed slurry passes through the membranes. All the components in this system are constructed of stainless steel 316. Figure 3.3 shows a schematic diagram of the nanofiltration system while Figure 3.4 shows the front view of the system itself.

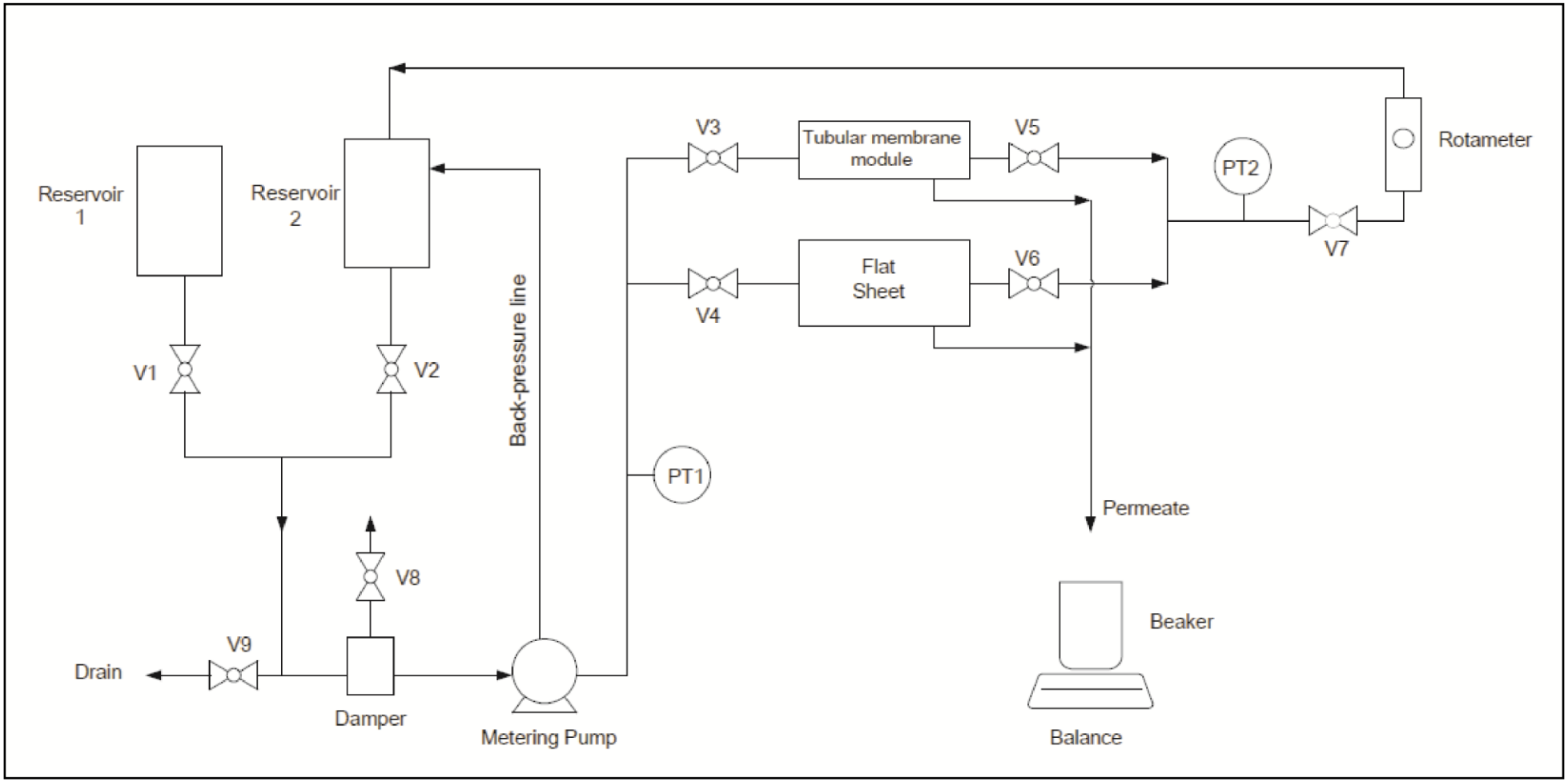


Figure 3.3: **Process flow diagram for membrane bench filtration unit (Model: TR 32)**
(Source: Department of Chemical Engineering, University of Malaya)

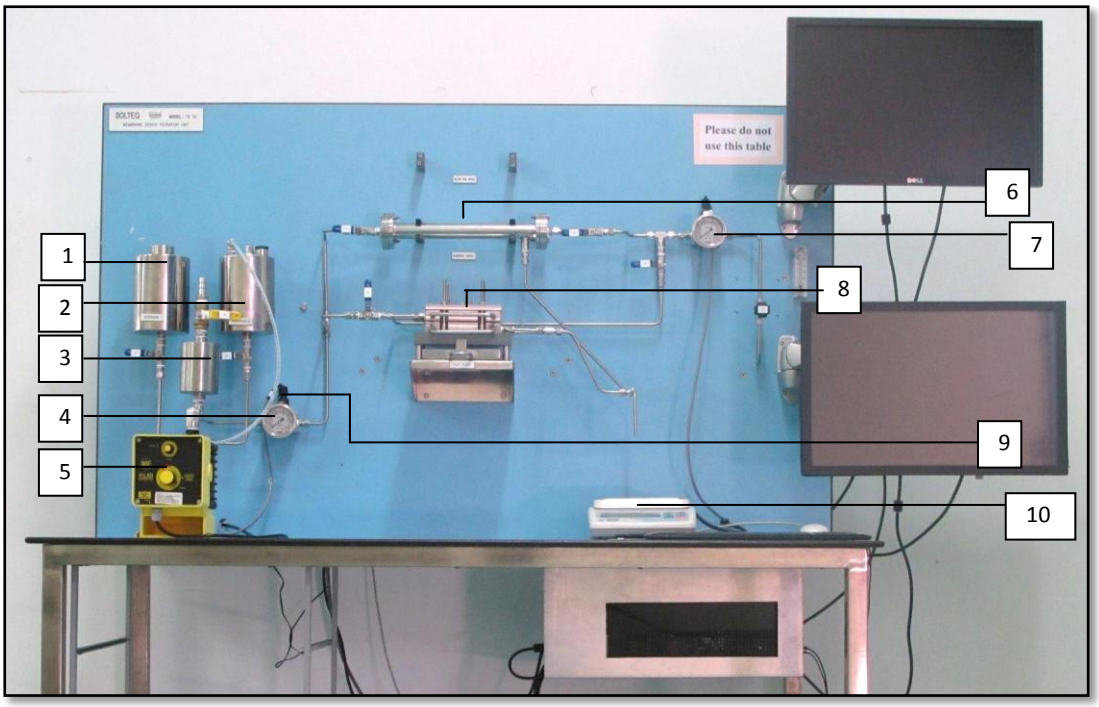


Figure 3.4: **Nanofiltration system Solteq-TR32 from Solution Sdn. Bhd**
(Source: Department of Chemical Engineering, University of Malaya)

Component List:

1. Reservoir tank 1
2. Reservoir tank 2
3. Dampener
4. Pressure gauge
5. Metering pump
6. Tubular membrane module
7. Pressure gauge
8. Flat sheet membrane module
9. Pressure transducer
10. Weighing balance

3.1.3 Preparation of sulphonamide solutions

500 mg/L of all sulphonamide stock solutions were prepared individually in a mixture of methanol and ultrapure water with 1:1(v/v) ratio. Ultrapure water produced from Milli-Q system (Merck, USA) was used to eliminate the contamination that could affect the experiment. Since sulphonamide is sensitive to light, in order to avoid possible photo-degradation, all sulphonamide stock solutions were put into amber bottles and stored at temperature below 4^{o}C. The stock solutions were renewed every month.

Hypochlorite stock solution however, was always prepared prior to the usage due to the instability of free active chlorine (FAC) in water. 1 g/L of FAC was prepared by diluting a purchased 4% sodium hypochlorite in ultrapure water. Concentration of FAC was determined by using HACH Chlorine Pocket Calorimeter II with a DPD reagent obtained from HACH (CO, USA).

To prepare all the working solution, further dilution of stock solution with ultrapure water is required. The concentration required can be achieved using a dilution equation which is:

$$\mathbf{M_i V_i = M_f V_f} \qquad \textbf{-Eq (3.1)}$$

where *M* is concentration of the solution, and *V* is volume of the solution while *i* is initial value and *f* is final value after dilution.

Working solutions of all sulphonamides were prepared to be within the range required (either for chlorination or nanofiltration) with less than 1% deviation.

3.2 Chlorination of sulphonamide

3.2.1 Kinetics of reaction between FAC and sulphonamide

Since the limitation of HPLC which can only detect up to 100 µg/L of by-products, higher concentration of precursor (sulphonamide) is required for good analysis. So in this case the concentration of 2.0 x 10^{-6} M sulphonamide was chosen. Fifty milliliter of sulphonamide working solutions with a concentration of 2.0 x 10^{-6} M were prepared in an amber glass bottle and stirred continuously with a Teflon-coated magnetic bars using magnetic stir-plate.

Temperature of the solutions was maintained at room temperature (25 ± 2°C) by partially immersing the amber beaker in a water bath. Three sets of each sulphonamide solutions were prepared in which the pH of each solutions were adjusted to 5.6, 7.2, and 10.0. These ranges of pH were chosen in this study because it covers the different charges of sulphonamide (neutral and negative) with pK_a value ~6. Fifty millimolar of phosphate buffer was added to maintain the pH of all sulphonamide solutions.

The chlorination process starts when an excess of FAC (at least 1:10 ratio of sulphonamide to FAC) is added into the working solution. One milliliter of sample was taken from the reaction mixture at fixed time intervals (30 s, 60 s, 150 s, 400 s, 1000 s, and 2500 s) into a 2 mL vial and was quenched immediately using a soft quenching technique (will be explained in section 3.2.2) to remove any residual FAC. Collected vials were subsequently sent to HPLC-UV for analysis with the purpose of monitoring the reduction in sulphonamide concentrations by FAC over time.

Reaction between sulphonamide and chlorination were modeled after the assumption of second order kinetics, that is, first order with respect to both chlorine and sulphonamide. However, since the chlorine was in excess during the analysis, the chlorine concentration remains constant throughout the reaction. Thus, a pseudo first order equation (Eq. 3.2) was used to calculate the experimental results of each derivative (Chamberlain & Adams, 2006; Gao et al., 2014). Results obtained were used to calculate the values of k' of each derivatives using the equation solver in Microsoft Excel.

$$\ln(Concentration(t) / Concentration(initial)) = -k't \qquad \textbf{-Eq (3.2)}$$

where k' is the pseudo first order rate constant and t is time (sec).

3.2.2 Transformation study of intermediate by-products

Studies done by Dodd & Huang (2004) shows that a reaction between FAC and sulphonamide produces an intermediate by-product (N-chlorinated sulphonamide) with the ability to retransform to parent compound in the absence of FAC. A quenching process with strong sulfur compound (which is usually employed by water and wastewater treatment plant for dechlorination process) would rapidly eliminate any residual FAC and would retransform the said compound to parent compound (Chamberlain & Adams, 2006; García-Galán, et al., 2008). This phenomenon will definitely affect the kinetic study of the chlorination process. Due to this reason, a soft quenching method proposed by Dodd & Huang (2004) was adopted for the chlorination study of sulphonamide. This method not only eliminates any residual FAC in the mixture but is able to prevent the intermediate by-product from retransforming to parent compound. However, in order to quantify the intermediate by-product, quenching process with sulfur compound (which, in this case is sodium sulfite) is necessary. The difference in concentration of sulphonamide between normal quenching and soft quenching would account for the concentration of N-chlorinated sulphonamide. This conclusion was made from the fact that only N-chlorinated sulphonamide could retransform to parent compound with less than 10% of that intermediate by-product being transformed to by-products (Dodd & Huang, 2004).

In the soft quenching technique, ammonium chloride (NH_4Cl) was used as a reductant. NH_4Cl reacts with residual FAC to form chloramines. At pH <5, chloramines react very slowly with sulphonamide (García-Galán, et al., 2008). Prior to sampling, a small volume of tris(hydroxymethyl) aminomethane (THAM) (~5 uL) was added with and NH_4Cl (~10 uL) in a vial. THAM was added in order to ensure that the pH after

sampling processes remain around pH 8.3 whereby at this pH value NH_4Cl has a higher reactivity to FAC compared to sulphonamide. Acetic acid was added later to maintain the pH between 4.5 and 5. This step would prevent N-chlorinated sulphonamide from re-transforming into parent compound. With this technique, the concentration of the sample could be preserved for about one hour from the start of the sampling process.

Using the same samples preparation procedure employed for the kinetic study, 50 mL solutions of buffered sulphonamide were prepared and subsequently subjected to chlorination process with 1 to 1 ratio of sulphonamide to FAC. However, after 10 minutes of reaction, one milliliter of the samples were quenched using sodium sulfite instead of soft quenching. For comparison, another one milliliter of the sample was taken and quenched using 'soft' quenching technique. All collected samples were sent for analysis by HPLC-UV and LCMS-IT-TOF. Experiments were repeated for other new samples but with an excess of FAC ([sulphonamide]: [FAC] <10).

3.3 Nanofiltration of Sulphonamide

Before installing the flat sheet TS80 polyamide composite membrane on the flat sheet membrane module, the membrane was soaked for 24 hours in deionized water and the water was changed every 8-12 hours with new deionized water. Prior to the nanofiltration process, preparation had to be done in three steps. The first step is to compact the membrane with ultrapure water at 5 bars until ultrapure water flux remained constant. The second step is to measure the water flux once the flux is stable for another 30 minutes and the final step is to substitute the reservoir filled with ultrapure water with the working solution. These three steps were employed every time nanofiltration process was used.

For nanofiltration process, sulphonamide working solutions with initial concentration of $2x10^{-5}$ M were prepared individually. Higher concentration of sulphonamide was used for nanofiltration study in order to improve the detection of intermediate and by-products so that the performance of nanofiltration membrane could be effectively determined. The pH of the sulphonamide working solution were varied at pH 5.6, 7.2, and 10.0 but no phosphate buffered was used for this experiment as it could significantly affect the permeate fluxes. Operating parameter for the whole experiment was fixed at 5 bars of pressure, 120 – 150 mL/min of flow rate in room temperature. These parameters were decided based on the suitable parameter setting for nanofiltration process using TR-32 Membrane filtration system and fixed so as not to affect the study on effect of other parameter. The solutions were stirred continuously throughout the experiments. Table 3.2 summarizes the operating parameters used for the nanofiltration processes throughout the entire research.

Table 3.2: Operating parameter for the nanofiltration system

Operating Parameter	Value
Membrane Effective Area	40.92 cm^2
Working Pressure	5 ± 0.2 Bar
Flow rate	120 – 150 mL/min
Temperature	25°C
Initial Concentration	2.0 x 10^{-5} M

Experiments started when an initial volume of 1.5 Liter working solution was subjected through the membrane. Prior to nanofiltration, one milliliter sample was taken from the feed water for measurement of the initial concentration. The system works in continuous mode where the unfiltered feed water would be returned to the reservoir for recycling. Experiment was stopped after 24 hours of experiment. At the end of the

experiment, one milliliter samples were taken from retentate and permeate solution and send for analysis using HPLC.

The nanofiltration processes were repeated using the same membrane until a total of ~120 hours of nanofiltration process was achieved. This was done in order to compare the fluxes and morphology of the membrane used in this part with the membrane used in other part of experiments (which were conducted with the same duration, ~120 hours). The other purpose was to prepare the filtrated feed for chlorination in post-chlorination study in section 3.4.3. New membranes were employed for each type of sulphonamide and a total of 3 replicates were done for each sulphonamide.

3.4 Combination of Chlorination and Nanofiltration for sulphonamide Removal.

For comparison purpose, experiments on combination of chlorination and nanofiltration of sulphonamide were divided into three parts; (1) Pre-chlorination-nanofiltration system (herein called the Pre-chlorination system) where the chlorination process was performed on the influent; (2) Simultaneous chlorination-nanofiltration (herein called the Hybrid system) where the chlorination process was performed during nanofiltration and (3) Post-Chlorination-nanofiltration (herein called the Post-chlorination) where the chlorination process was performed on the effluent after nanofiltration. The testing procedure for this part of experiment is summarized and shown in Figure 3.5.

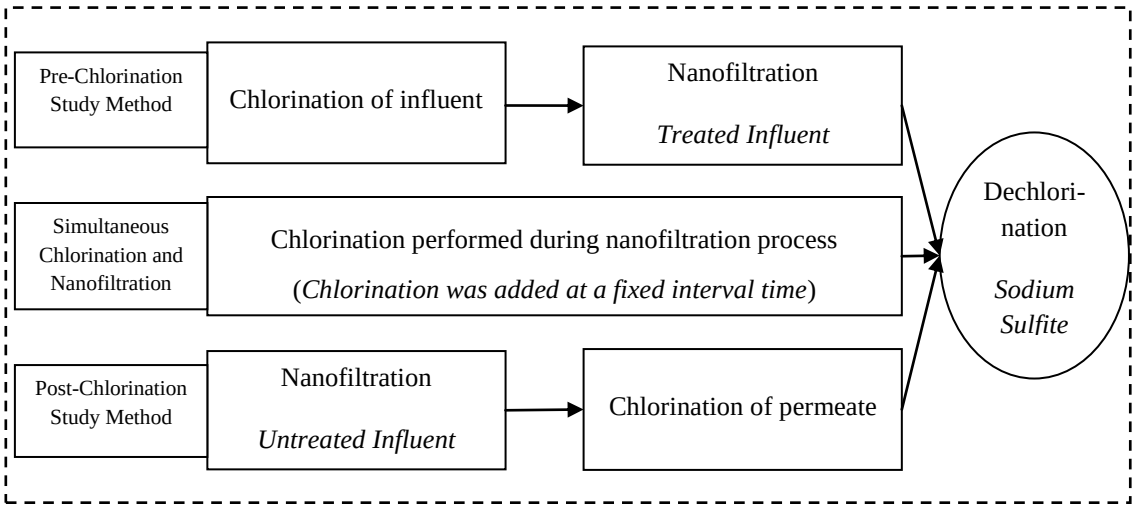


Figure 3.5: Testing procedure used for nanofiltration studies

3.4.1 Chlorination followed by Nanofiltration (Pre-chlorination)

In the Pre-chlorination system, chlorination process was done to the sulphonamide feed solution before the nanofiltration. The same procedure of preparing the working solution for nanofiltration of sulphonamide in section 3.1.3 was employed in preparing the feed solution. Pre-chlorination process begun when an excess FAC [4.0×10^{-5} M (3.00 mg/L)] was added to the continuously stirred 1.5 Liter feed solution. A minimum of 30 minutes contact time was allowed to ensure that complete reaction between FAC and sulphonamide will be achieved (Chamberlain & Adams, 2006). FAC residual, concentration of residual sulphonamide and its by-products were measured afterward. The pre-treated feed solution was then subjected to nanofiltration for 24 hours. Final concentration of FAC, sulphonamide and its by-products were measured and compared with the initial feed. By using the same membrane, the experiments were repeated using new batches of pre-treated feed water until a total of ~ 120 hours of experiments was conducted. For each type of sulphonamide tested, a new membrane was applied. Experiments were repeated but this time by using a feed solution treated with a limited concentration of FAC [4.0×10^{-6} M (0.3 mg/L)].

3.4.2 Simultaneous Chlorination and Nanofiltration

In the hybrid system, chlorination process was performed simultaneously with the nanofiltration process. Throughout the entire nanofiltration process, a concentration of 2 mg/L FAC was spiked for every 60 minutes into a 1.5 Liter of feed solution. Based on the trial and error done on the chlorination of sulphonamide for one hour, 2 mg/L concentration of FAC was considered enough (in excess) for a complete reaction with sulphonamide every hour without leaving too much residual FAC (below ~1 ppm). One milliliter of permeate was taken at every two hours prior to the spiking of FAC and the collected samples were analyzed using HPLC. Since measurement of FAC required a higher volume of permeate (at least 10 mL per testing), FAC measurements were only done to permeate after every 800 mL of permeate was collected so as not to affect with the other results. To maintain a constant working volume of the system, a constant rate of sulphonamide was fed from an independent reservoir tank into the feed reservoir. The process was stopped after 120 hours of experiment. Like the other two systems, new membranes were used for each type of sulphonamide tested.

3.4.3 Nanofiltration followed by Chlorination (post-chlorination)

As for the post-chlorination system, no additional nanofiltration process was required as the 1.5 L of permeate collected from the nanofiltration of sulphonamide in section 3.3 is deemed suitable to be used. For comparison purpose, the same concentrations of FAC used in pre-chlorination system (both limited and excess FAC) was applied to the permeate solution. The mixture was stirred continuously until the mixture is fully reacted (~30 minutes) and then the residual FAC, sulphonamide, and its by-products were measured and compared with the other systems. All the three systems were

replicated three times and were compared in terms of fluxes performance, rejection of sulphonamide and its by-products.

3.5 Analytical Methods

3.5.1 HPLC-UV

The method employed in this experiment to determine the changes in concentration of sulphonamide in samples was an improved version of the method developed by Hartig (1999) using high performance liquid chromatography (HPLC-UV). This method eliminates the requirement for buffer as a mobile phase and reduces the amount of time required for each analysis. It also increases the distance (retention time) between compounds for easier identification of reaction by-products.

The detection wavelength used for all four sulphonamide was set at 272 nm. However, the column used were different from the said literature review because the new column used in this experiment (i.e. 150 mm L x 4.6 mm I.D. ODS Hypersil with 5.0 µm particle size) from Thermo Fisher (MA, USA) offer shorter analysis time by 20% when used with the same operating parameter. Column temperature was maintained at 35°C. The mobile phase used was ultrapure water with 0.1% Formic Acid (A) and pure Acetonitrile (B) in gradient mode with a flow rate of 1 mL/min. Gradient elution started with 90% of A and decreased to 40% in 30 minutes then further decreased to 10% in 5 minutes. From there, A was held for about 5 minutes and rapidly increased back to 90% within 1 minute. Re-equilibration of the column took 5 minutes before the next analysis could be done. A total of 46 minutes was required for analysis of each sample. Figure 3.6 shows the gradient elution curve of mobile phase used for HPLC.

The standard calibration curves for four types of sulphonamide were prepared by diluting its respective stock solution with ultrapure water. Ten known concentration of sulphonamide were prepared ranging from 600 ng/L, 700 ng/L, 1 µg/L, 10 µg/L, 40 µg/L, 70 µg/L, 100 µg/L, 400 µg/L, 700 µg/L, and 1 mg/L. All of these samples were sent to HPLC-UV for analysis. From the value of absorbance obtained from analysis for all known concentration, standard calibration curve for each sulphonamide were plotted (Appendix A).

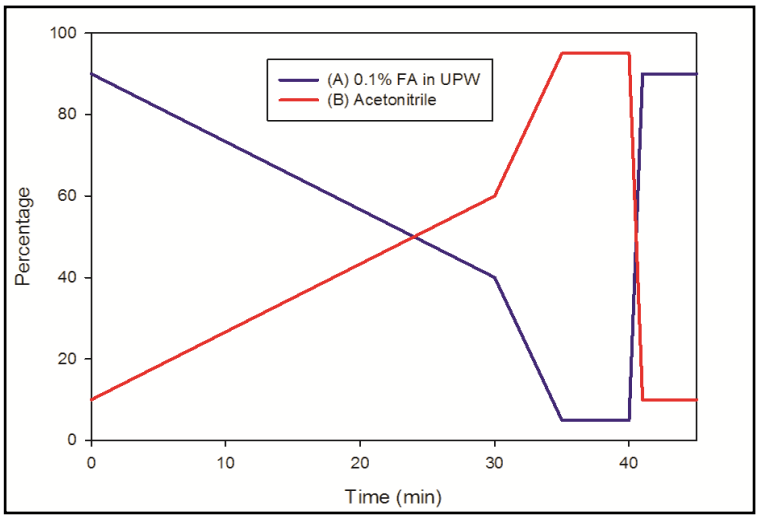


Figure 3.6: **HPLC mobile phase gradient elution curve**

3.5.2 LC-TOF-MS

In order to identify the accurate mass and possible molecular structure of the reaction by-products from chlorination process of sulphonamide, LCMS-IT-TOF Prominence Series (Shimadzu, Japan) was used. The same parameters and column that was used for HPLC-UV analysis was used for this system. A scan range was set to 50-1000 m/z for analysis using 120eV fragmentation voltages. Nitrogen generated nebulising gas flow was configured to 1.5L/min while the Curved Desolvation Line (CDL) temperature and heat block temperature were set to 250°C and 200°C, respectively.

3.6 Data analysis of nanofiltration performance

Performance of nanofiltration membrane can be expressed in terms rejection of sulphonamide and its by-product and flux.

3.6.1 Rejection

The total amount of substance removed from feed solution by the membrane is called "Rejection" and is expressed as percentage of rejection which is can be calculated by using formula:

$$\%\ \boldsymbol{Rejection} = \frac{\boldsymbol{Feed\ Concentration - Permeate\ Concentration}}{\boldsymbol{Feed\ Concentration}} \times \mathbf{100}\% \qquad \textbf{-Eq (3.3)}$$

where "Feed Concentration" is the initial amount of substance in the feed solution entering into the membrane module while "Permeate Concentration" is the amount of substance in the exit stream.

3.6.2 Flux

In membrane filtration, flux ($L/m^2.h$) can be termed as a volume of feed that passes through the membrane effective area within a specified duration. The calculation is as below:

$$\boldsymbol{Flux} = \frac{\boldsymbol{Volume\ of\ permeate(L)}}{\boldsymbol{Membrane\ effective\ area\ (m^2)}} \times \boldsymbol{1/time(h)} \qquad \textbf{-Eq (3.4)}$$

The volume of permeate was obtained by converting the weight measurement assuming that the density of permeate is 1 g/mL at 1 atm.

CHAPTER 4

RESULTS AND DISCUSSION

All the experimental data that were collected from this research are analyzed and presented in this chapter. The discussion on the results started with the optimization of the analytical equipment (HPLC) followed by the preliminary study on the effect of chlorination process to the degradation of sulphonamide antibiotic. Performance on different modes of arrangement between nanofiltration and chlorination are the main focus of this study and are explained in detail in this chapter. Comparison was done between all of the treatment modes involved in order to determine the most effective method to treat sulphonamide.

4.1 Analysis of Sulphonamide using High Performance Liquid Chromatography

4.1.1 Retention Time

Concentrations of sulphonamide in samples were measured by using High Performance Liquid Chromatography (HPLC). Figure 4.1 shows the spectrum result of the analysis for the mixture of all four sulphonamide derivatives. The HPLC spectrum of sulphonamides tested were separated by different retention time, which is summarized in Table 4.1.

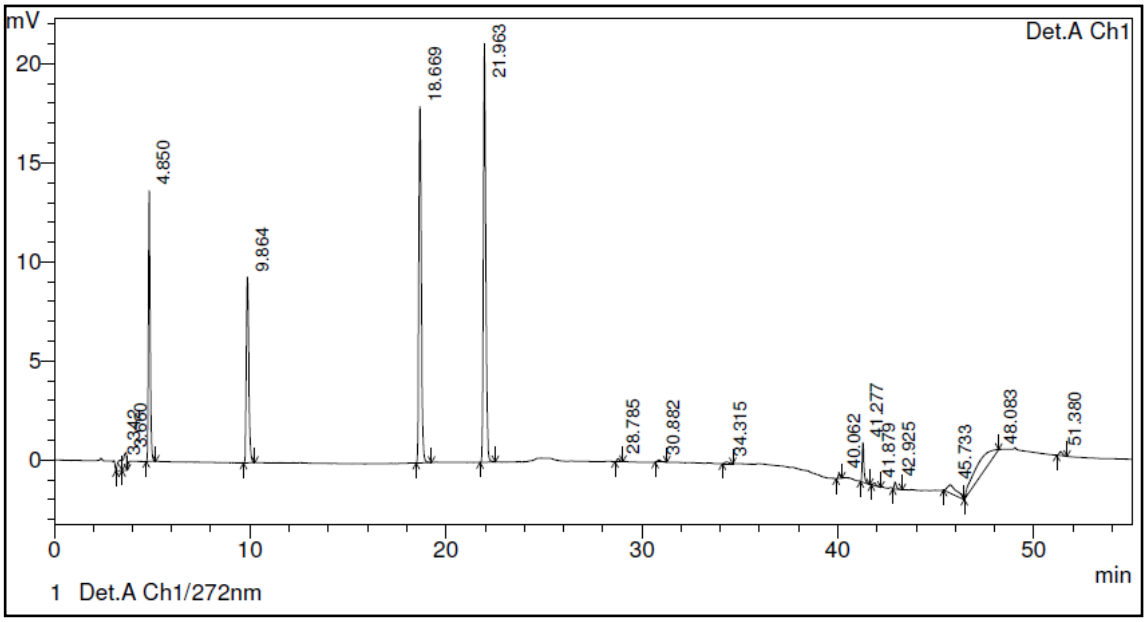


Figure 4.1: **HPLC Spectrum for four sulphonamide derivatives studied on wavelength 272 nm [C_0 = 2 x 10^{-6} M].**

Table 4.1: **Retention time recorded from HPLC for each sulphonamide derivative.**

No.	Sulphonamide	Retention time(m)
1	Sulfanilamide	4.850
2	Sulfadiazine	9.864
3	Sulfamethoxazole	18.669
4	Sulfadimethoxine	21.963

4.2 Chlorination of Sulphonamide

4.2.1 Effect of pH on Chlorination Process of Sulphonamide

In order to understand the reaction kinetic between sulphonamide and FAC, the experiments were conducted at 3 different pH values, which are pH 5.6, 7.2 and 10.0. Samples were collected at fixed intervals and were then measured using HPLC. For each type of sulphonamide derivative, a total of 9 samples were taken for analysis. The results obtained were plotted and are shown in Figure 4.2. Based on the pK_a value of all sulphonamide studied (5.9 to 10.1), these range of pH were chosen in this study because it covers the different charges of sulphonamide (neutral and negative) which is

important in understanding the interaction between charged sulphonamide and the charged surface of nanofiltration membrane in later studies.

Even though the concentration of sulphonamide between each derivatives in Figure 4.2 were found to be reduced at different rates, the results show a similar trend whereby the concentration of all sulphonamide decrease rapidly for the first 360 seconds (1^{st} to 5^{th} samples) and then the reaction slowed down until it reached zero. Since the FAC concentration added was in excess, the reduction in reaction rate over time was due to the reduced number of sulphonamide compound available for the reaction. Among the entire sulphonamide derivative studied, SDM was found to degrade the fastest where completed reaction was achieved in less than 150 seconds compared to SNM, SDZ, and SMX which only achieved full degradation after 400, 2500, and 1000 seconds, respectively. The differences in molecular structure between each sulphonamide derivatives contribute to the different degree of degradation for sulphonamide derivatives. Detail discussion on the different reactivity between sulphonamide derivatives with chlorine is further discussed in section 4.2.2.

It is also observed that the reaction rates deviated significantly with the changes of pH. Increasing the pH of the reaction caused the reaction rate to be reduced. For example, chlorination of SNM at pH 5.6 and 7.2 showed completed degradation at much earlier reaction time before 400 seconds compared to the reaction at pH 10 which was fully degraded after 1000 seconds. In addition, there is not much difference in reaction rate between pH 5.6 and 7.2 except for the slightly higher rate observed at pH 5.6. The same patterns were also detected for other sulphonamide derivative where the reaction at pH 5.6 is faster compared to pH 7.2 and 10.0.

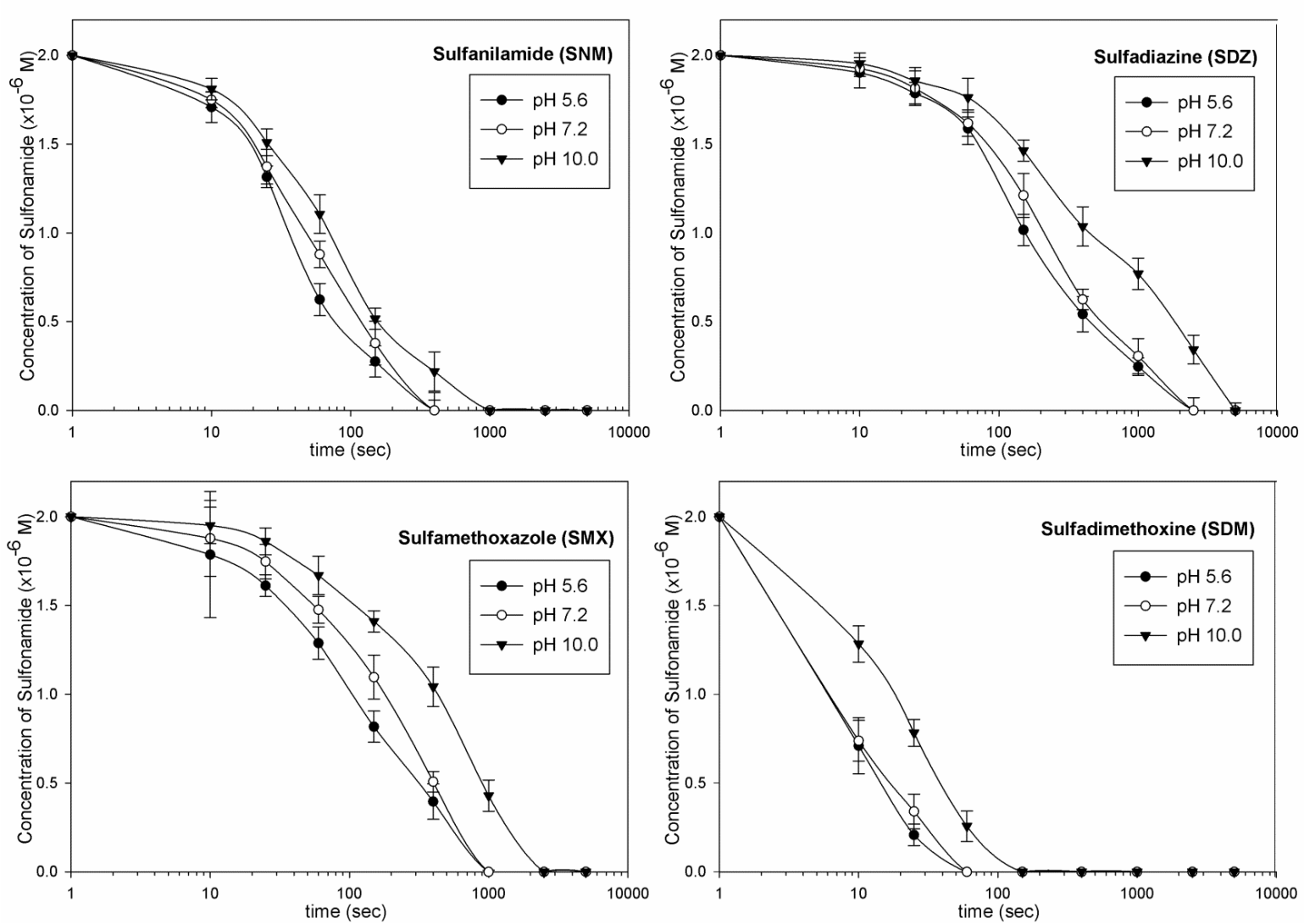


Figure 4.2: **Substrate losses of sulphonamide by chlorination process [2.0 x 10^{-5}M of FAC] in phosphate buffered solution at 3 different pHs**

The reaction between sulphonamides and FAC were actually evaluated based on the contribution of both sulphonamide and FAC concentration at different pH. Several studies have shown that both sulphonamide and FAC speciated differently at different range of pH (Deborde & von Gunten, 2008; Z. Qiang & C. Adams, 2004). Based on Figure 2.3 in Chapter 2 literature review, the dissociation equilibrium of sulphonamide showed that the sulphonamide has three species, namely, anionic, neutral and cationic sulphonamide. A speciation study by Sakurai & Ishimitsu (1980) on various sulphonamides showed that less than 2 percent of the neutral species of sulphonamide were zwitterionic. Furthermore, the presence of cationic sulphonamide only exists greatly at a very low pH (pK_a~ 2), which is not included in the range of pH studied and thus only anionic species of sulphonamide were considered for reaction (Z. Qiang & C. Adams, 2004; Z. Qiang & C. D. Adams, 2004).

As for the speciation of chlorine, FAC with pK_a value of 7.5 at 25°C may exist as hypochlorite ion (ClO^-) or as hypochlorous acid (HOCl), depending on the pH of the solution (Deborde & von Gunten, 2008). The fraction of both chlorine species as a function of pH could be calculated from the Equation 4.1 (Deborde & von Gunten, 2008):

$$\alpha OCl^- = [1 + (10^{-7.5} \times 10^{pH})]^{-1} \quad \textbf{- Eq. (4.1)}$$

where αOCl^- is the fraction of free chlorine in hypochlorite form and $\alpha HOCl$ is another fraction of free chlorine in hypochlorous acid form.

According to Deborde & Von Gunten (2008), the relative distribution of chlorine species at various ranges of pH is as shown in Figure 4.3. Hypochlorous acid (HOCl) exists as dominant species in the acidic region while hypochlorite ion (ClO^-) in the basic

region with pH 7.5 acting as equilibrium between these two species. Since only the presence of anionic form of sulphonamide was considered significant in this study, reactivity of the reaction is closely dependant to the various chemical form of aforementioned hypochlorite at different pH.

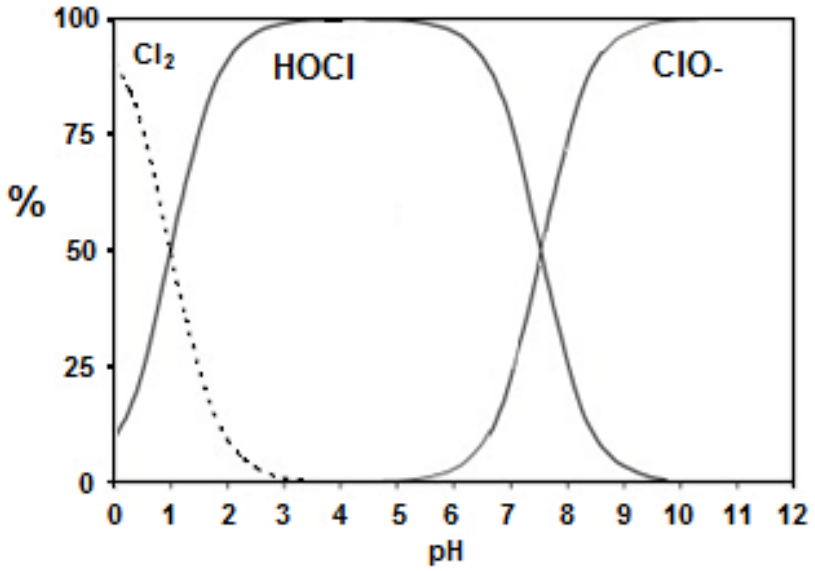


Figure 4.3: **Fraction of chlorine species as a function of pH at 25°C**
(Source: Deborde & von Gunten, 2008)

Based on the result obtained (Figure 4.2), the concentration of all sulphonamide derivatives were found to react faster with FAC in acidic region compared to neutral and basic region. This observation suggests that the reactions that occur are mainly dominated by reactions between sulphonamide and hypochlorous acid rather than hypochlorite ion. Similar phenomenon was also observed in published literature stating that hypochlorous acid is the primary oxidant species present in FAC while hypochlorite ion does not significantly contribute to the reaction (Chamberlain & Adams, 2006; Gao, et al., 2014). Another study done by Dodd & Huang (2004) on chlorination of sulfamethoxazole (SMX) also showed that the anionic species of SMX was twice as reactive with hypochlorous acid compared to its neutral species. This finding is actually applicable to other derivatives of sulphonamide because of the

similarity in chemical structure commonly found among all sulphonamide derivatives which is p-aminobenzenesulphonamide moiety (Dodd & Huang, 2004).

4.2.2 Reactivity of Sulphonamide during Chlorination Process

Reaction between sulphonamide and chlorination were actually modeled after the assumption of second order kinetics, that is, first order with respect to both chlorine and sulphonamide. However, to observe the reactivity of sulphonamide, chlorine was supplied in excess during the analysis so that the chlorine concentration remains constant throughout the reaction. Thus, pseudo first order equation (Eq 4.2) was used to analyze the experimental data where k' is the pseudo-first-order constant (Chamberlain & Adams, 2006).

Table 4.2: Pseudo first order value, k' and coefficients of determination, R^2 for chlorination of sulphonamide in ultrapure water at pH 5.6, 7.2, and 10.0 at T = 25°C.

pH	pH 5.6		Ph 7.2		pH 10.0	
Compound	k' (s^{-1})	R^2	k' (s^{-1})	R^2	k' (s^{-1})	R^2
SNM	0.0141	0.9541	0.0115	0.9837	0.0092	0.9957
SDZ	0.0034	0.9749	0.0030	0.9944	0.0017	0.9827
SMX	0.0044	0.9357	0.0035	0.9864	0.0017	0.9478
SDM	0.0923	0.9911	0.0748	0.9546	0.0349	0.9931

$$\ln(Concentration(t) / Concentration(initial)) = -k't \quad \textbf{-Eq (4.2)}$$

where k' is the pseudo first order rate constant and t is time (sec).

Table 4.2 summarized the pseudo first order rate constants for all tested sulphonamide. From the value of k' calculated, removal of sulphonamide in ultrapure water was confirmed to follow the pseudo-first order reaction with $R^2 > 0.9357$.

A comparison on the reaction rate between the four derivatives of sulphonamide studied can be seen clearly from the pseudo first-order plots in Figure 4.5. Among the three pH studied, data obtained from reaction at pH 7.2 with excess FAC (ratio [1:10] sulphonamide against FAC) was taken for comparison purpose. From the first order plot of chlorination kinetics, the reactivity of sulphonamide with free chlorine can be arranged from highest to lowest as follows: SDM > SNM > SMX > SDZ. Evidently the differences in reaction rate found between sulphonamide derivatives were not related to the molecular weight of the compounds as SNM the compound with the smallest molecular weight have a higher reaction rate compared to both SDZ and SMX where both have higher molecular weight compared to SNM. One of the most probable factors that affect the reaction rate between sulphonamide derivatives is molecular structure.

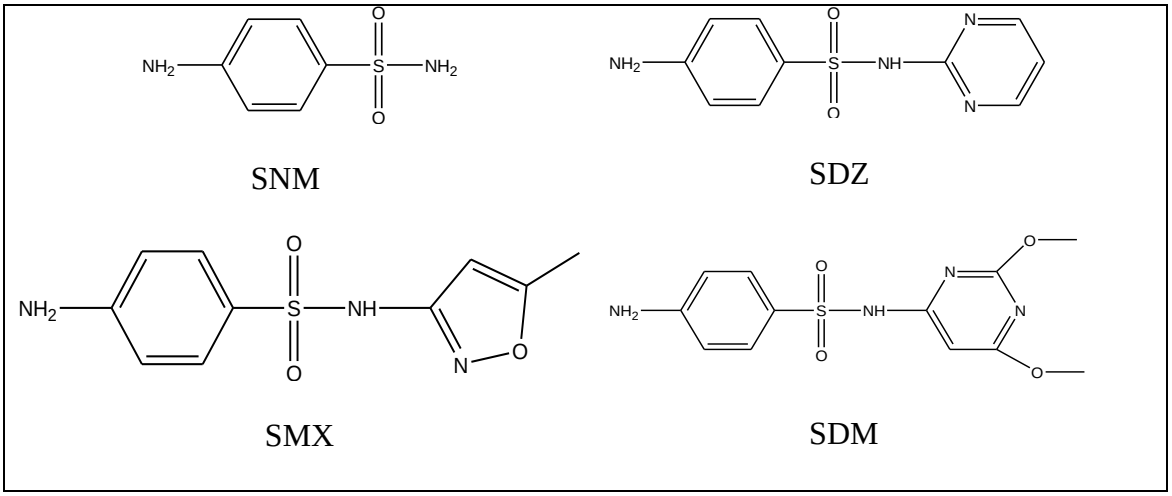


Figure 4.4: **Chemical structure of sulphonamide derivative used in this study.**

From the chemical structure on Figure 4.4, except for SNM, we can see that all sulphonamide derivatives have benzene rings structure. Smaller chemical structure of

SNM may result in a fast reaction compared to the other sulphonamide. Furthermore, SDZ and SMX share almost similar structure except for the differences in one molecule in the benzene rings where oxygen compound is in SMX while nitrogen compound is in SDZ. This is probably the reason why these two showed almost similar reactivity towards chlorine. As for SDM, two oxygen molecules attached to the benzene ring are susceptible to chlorine attack and thus resulted in a very fast reaction compared to the other three sulphonamides. However, no previous literatures have been done to support this.

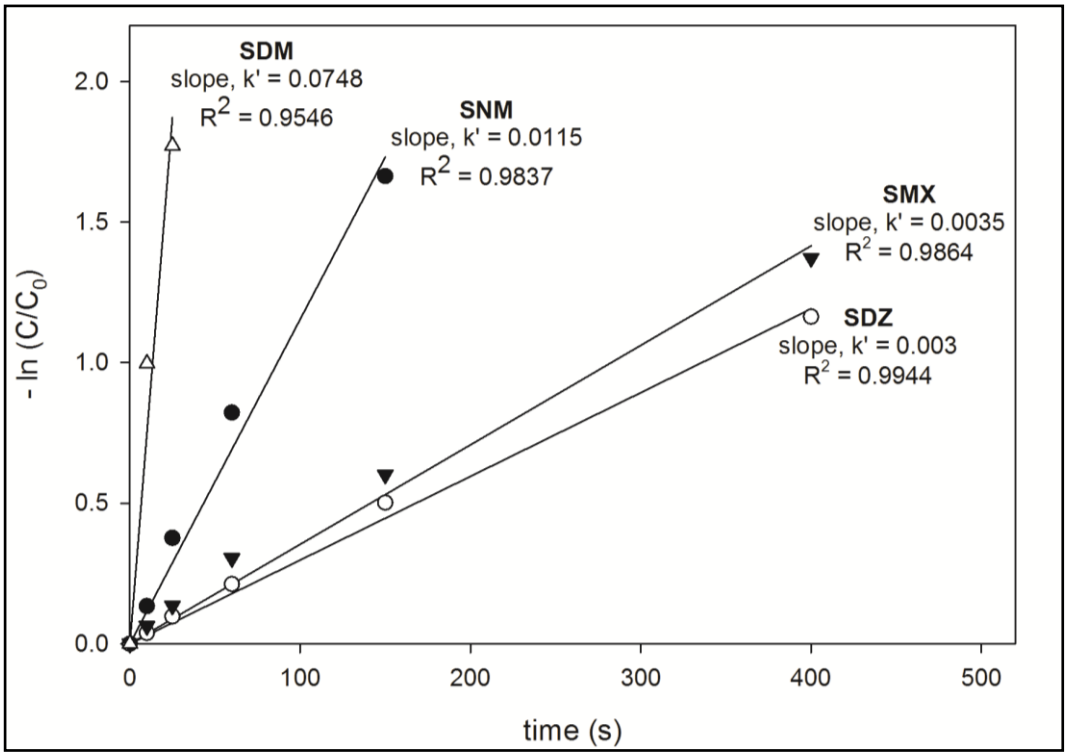


Figure 4.5: **Pseudo first-order plot of four sulphonamide derivatives oxidation kinetic with FAC in phosphate buffer solution pH 7.2, T=25^{0}C. ([FAC]$_0$ = 2.0 x 10^{-5} M, [Substrate]$_0$ = 2.0 x 10^{-6} M).**

From the k' value, pseudo-first order reactions were found to be higher in magnitude compared to the previous studies done elsewhere on various sulphonamide derivatives (Chamberlain & Adams, 2006). The rate constants obtained from this experiment exceeded more than a factor of 3 for both SMX and SDM under the same condition except for the type of quenching agent used. The differences in quenching agent used in

dechlorination process may be the factor that contributes to the different results. As mentioned in Chapter 3, the dechlorination process was done in order to observe the behavior of sulphonamide for situations in water treatment where residual chlorine maybe depleted, such as at the end of the consumer pipeline and also during dechlorination of wastewater treatment plant effluent. According to the study done by Dodd & Huang (2004), N-chlorinated sulfamethoxazole was an intermediate by-product that formed from the reaction between FAC and sulfamethoxazole. This compound has the ability to retransform to the parent compound (sulfamethoxazole) in the absence of free active chlorine. The normal quenching method used in other study (which typically employed in water and wastewater treatment plant to remove or reduce chlorine residual prior to effluent release) used strong sulfate compound that would rapidly retransform all N-chlorinated sulphonamide intermediate by-products to the parent compound thus increasing the sulphonamide concentration upon analysis.

In order to differentiate between the two methods of quenching used, all four tested sulphonamides underwent the dechlorination process where the compound was quenched with both sulfur compound (normal quenching) and chloramines (soft quenching) at two different concentration of FAC (limited vs. excess). Figure 4.6 shows the changes in concentration of sulphonamide after the dechlorination process according to the different type of quenching agent and initial concentrations of FAC used. It can be observed that the final concentration of sulphonamide derivatives increased after dechlorination using soft quenching in both limited and excess FAC. This phenomenon was caused by the retransformation of one particular intermediate by-product, namely N-chlorinated sulphonamide. Normal quenching was used as a baseline for the measurement of N-chlorinated sulphonamide where the different in final concentration of sulphonamide derivatives between normal quenching and soft quenching were

expected to be N-chlorinated sulphonamides due to the fact that only those compounds could retransform to the parent compound after FAC depleted or removed (Díaz-Cruz, et al., 2008; Dodd & Huang, 2004).

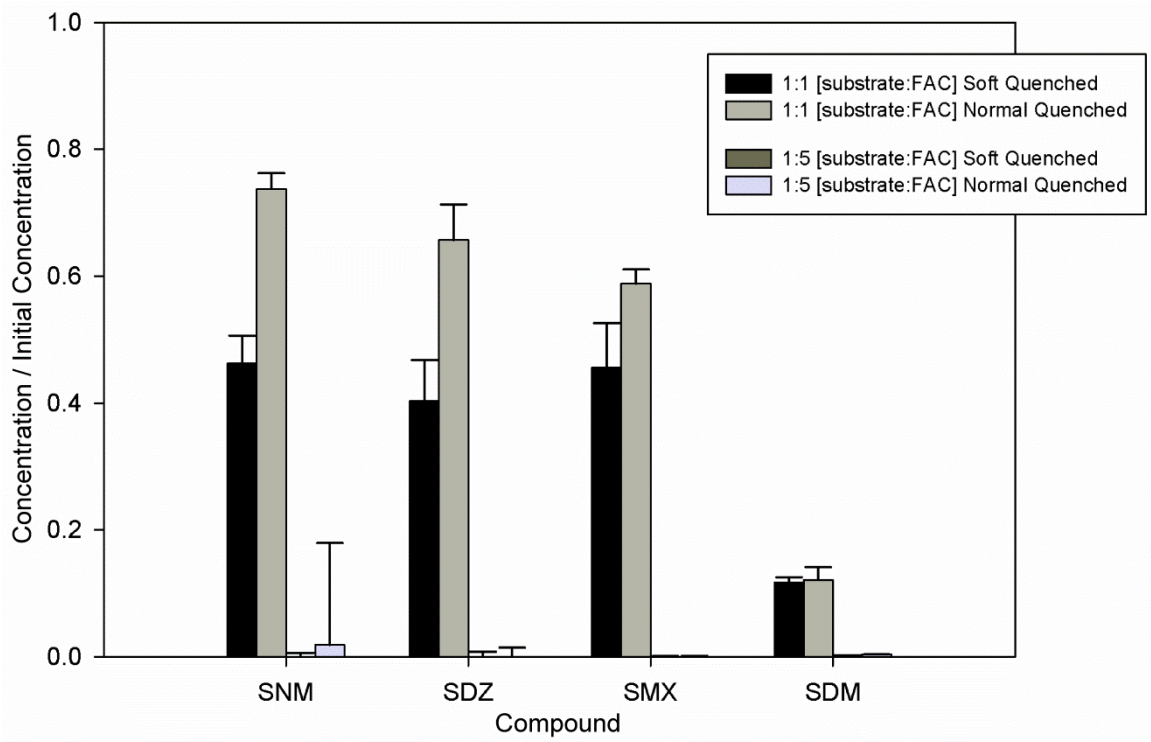


Figure 4.6: **Effect of dechlorination process (soft vs. strong) on retransformation of intermediate by-product to parent compound. The reactions were done individually.**

In the case of low concentration FAC was added, about 3 to 18% differences in sulphonamide concentration were observed to retransforms to their respective parent compounds, with SNM being the highest followed by SDZ. However when reacted with excess FAC, the concentration of N-chlorinated sulphonamides were found to be reduced. Residual chlorine in excess FAC will further reacted with N-chlorinated sulphonamide to form another by-product, N-N-dichlorinated sulphonamide and thus reducing the amount of N-chlorinated sulphonamide left to retransform to the original compound (Dodd & Huang, 2004). An example on schematic diagram of reaction pathway for the chlorination of sulfamethoxazole (SMX) is shown in Figure 4.7.

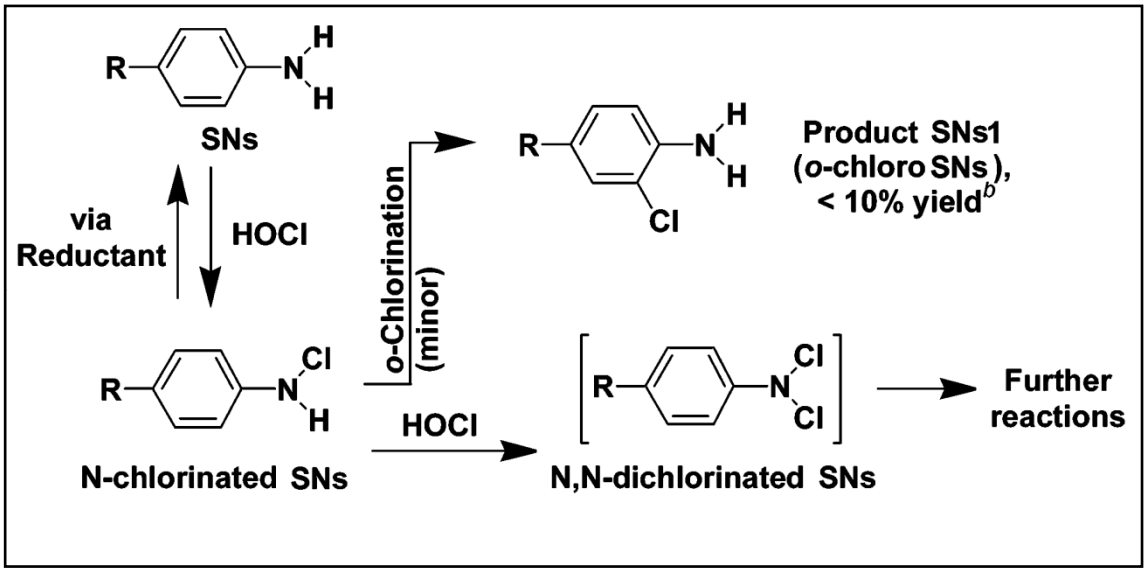


Figure 4.7: **Schematic diagram of reaction pathway for the chlorination of sulfamethoxazole with FAC.**
(Source: Dodd & Huang, 2004)

Although the soft quenching method is useful in preserving the intermediate N-chlorinated sulphonamides by-product, the chloramines present in the quenching agent would react extremely slow with residual sulphonamide and thus decrease the concentration of sulphonamide (Dodd & Huang, 2004; Gao, et al., 2014). However, the authors suggested that as long as the analysis could be completed within one hour after soft quenching, no significant changes that affect the measurement of final concentration of sulphonamide will occur. The finding of this study will be useful in explaining the performance of nanofiltration in removing chlorinated-sulphonamide in later section.

4.2.3 Analysis of Reaction Intermediate and By-products.

The intermediate and by-products detected by LC-TOF-MS are tabulated in Table 4.3. Peaks of the compounds observed with LC-TOF-MS were identified and then compared to the peaks obtained using HPLC and the molecular weight of each peaks were then arranged according to their respective peaks shown in HPLC spectra. This

information on molecular weight of chlorinated by-product of sulphonamide will be useful in determining the performance of nanofiltration system in removing the by-product of the reaction in later section.

Table 4.3: Mass ratio for chlorinated by-product of sulphonamide quenched using soft quenching method.

Parent Compound	T_R (min)	$M+[H]^+$	MS/MS
Sulfanilamide (SNM)	4.853	174.261	93.18
	9.521	99.720	72.11
	13.385	207.377	173.22
Sulfadiazine (SDZ)	3.737	187.356	170.38, 108.22
	8.120	251.399	156.22, 108.19, 92.17
	9.429	99.721	72.11
	14.202	285.413	142.22, 158.22, 250.39, 287.418
	19.652	385.556	231.33, 287.47, 185.32
Sulfamethoxazole (SMX)	9.411	99.721	72.11
	13.988	141.515	52.88,113.45,141.52
	15.640	254.796	108.91, 160.04, 194.02, 256.44
	18.341	288.199	126.34,142.22,158.22
	22.283	288.406	119.24, 159.91, 253.86, 146.29
	33.113	501.125	410.91,437.44
Sulfadimethoxine (SDM)	7.367	247.450	232.41, 174.05, 18.10, 201.30
	12.760	383.517	351.49, 156.22
	16.078	365.450	156.22
	18.770	311.500	108.10, 156.81, 218.76, 245.35
	22.317	284.398	161.23, 125.13, 252.34
	25.432	109.661	89.66, 212.22, 562.95

Overall, this preliminary study on chlorination of sulphonamide derivatives concluded that the pH value of the solution affects the reaction rate between chlorine

and sulphonamide where the reaction is much faster at lower pH. Based on the analysis of sulphonamide by-products, majority of the chlorination by-products of sulphonamide derivatives are higher in molecular weight compared to their respective parent compound. Since molecular size is one of the factors that affecting the performance of nanofiltration membrane (steric hindrance), these by-products will definitely affect the nanofiltration process in some way.

4.3 Preliminary Rejection of Sulphonamide by Nanofiltration Membrane Only.

4.3.1 Preliminary rejection of sulphonamide.

The concentration of sulphonamides regularly detected in water and wastewater influents in Malaysia, usually ranged between 5.12 ng/L to 94.95 ng/L(Malintan & Mohd, 2006). However, the concentrations of sulphonamide used for this study were increased a million fold (to mg/L). Due to the limitation of HPLC analytical instrument in measuring concentration that is below than ~100 µg/L, high concentration of sulphonamide is required so that the reaction by-product from the reaction between FAC and sulphonamide will be higher than the limit of detection for HPLC analysis.

In the preliminary study, the rejection of sulphonamide via nanofiltration only was conducted using feed water containing $2x10^{-5}$ M of non-buffered sulphonamide at pH 5.2, 7.2, and 10 under a pressure of 5 Bar sulphonamide influent feed. The results obtained were shown in Figure 4.8. Note that the filtration processes were done separately for each derivatives of sulphonamide. After 24 hours of experiment, with an exception to the SNM, high rejections of sulphonamide were achieved for all pH studied and. For example, the removal rate of 15.7%, 69.2%, 75.4%, and 79.0% was achieved at pH 7.2 for SNM, SDZ, SMX and SDM, respectively. Similar trends of

rejection for all sulphonamide derivatives were also observed on the other two pHs studied.

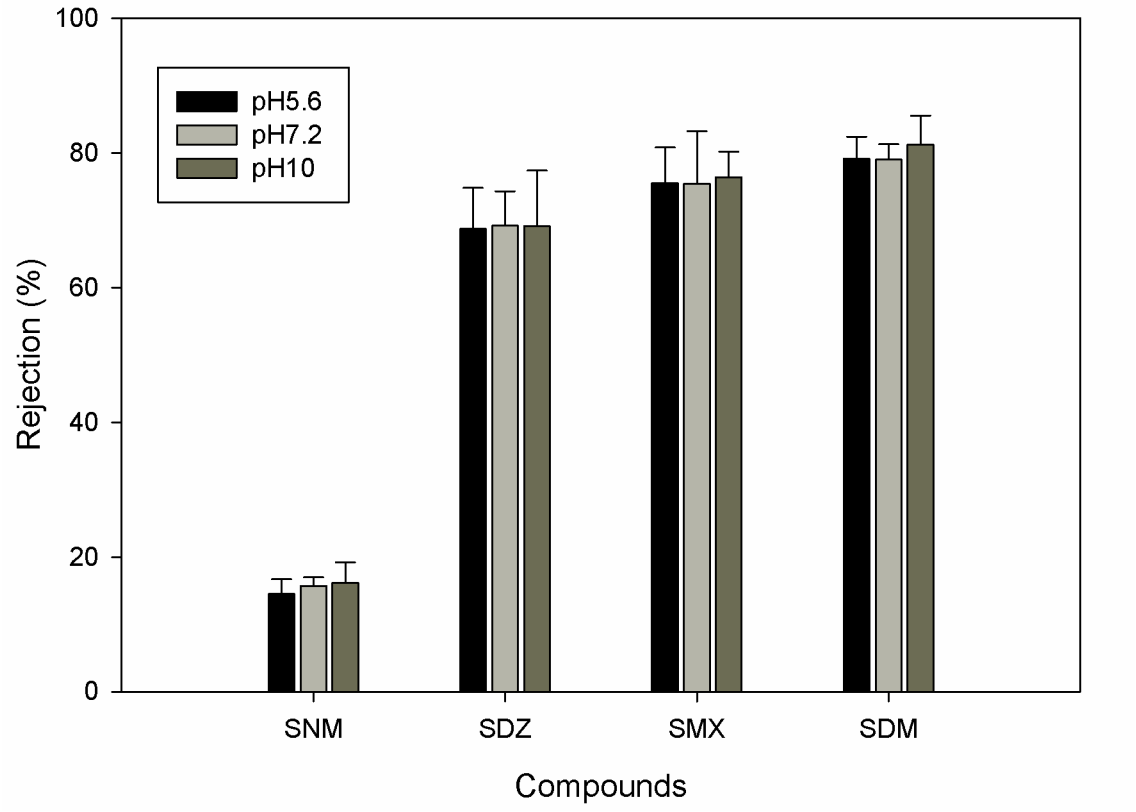


Figure 4.8: **Rejection of sulphonamide by pristine TS80 membrane at three different pH (pH 5.2, 7.2, and 10.0) at T = 25ºC after 24 hours.**

As all the compounds belongs to sulphonamide group have the same functional group (sulfonyl group attached to the amine group) (García-Galán, et al., 2008), the diversity found in rejection rate between the studied compound are closely related to the differences in molecular weight due to different organic group attached to certain sulphonamide. Compound with a higher molecular weight would have a higher rejection rate (with the assumption of no or smaller differences in charge repulsion) because of size exclusion in membrane sieving mechanism. Aside from SNM with molecular weight of only 172 g/mol, SDZ, SMX, and SDM with their respective molecular weight of 251, 253, and 311 g/mol have a larger molecular size than the molecular weight cut-off (MWCO) of the membrane (200Da), hence the increased in

rejection rate with SDM being the highest. Similar observation were also found on previous study conducted by Koyuncu et al. (2008) and Dolar et al. (2011) on removal of SMX in distilled water where approximately 60% of SMX were removed using NF200, a nanofiltration membrane with comparable properties with TS80 membrane.

It is also observed that the removal rates deviated with the changes of pH where slightly higher rejections of sulphonamide were achieved at higher pH value. As the charges of sulphonamide compound are dependent on the pH of the solution, the interaction between charges sulphonamide with membrane surface at different pH might affect the rejection process (Bellona & Drewes, 2005). However, all sulphonamides are neutrally charged at pH 5.6, but the rejections of sulphonamide at this pH were found to be similar with the rejections of negatively charged sulphonamide (with pK_a around ~6 except for SNM) at pH 7.2 and pH 10. Furthermore, with pKa value of 10.1, SNM are neutrally charged at all three pH, thus no charge repulsion exists between SNM and the membrane surface that could further improve the rejection. Evidently, charge repulsion did not play significant role in removing sulphonamide using nanofiltration membrane.

4.3.2 Membrane fluxes

Nanofiltration processes were repeated for a few times until a total of 120 hours of filtration was achieved. A final normalized flux values for every membranes used in this nanofiltration were collected and is tabulated in Table 4.4

Based on the observation of fluxes reading in Table 4.4, we can see that the normalized fluxes for the membrane used in nanofiltration of sulphonamide derivatives decreased significantly. More than 20% fluxes dropped from the initial value after 120 hours of filtration. Accumulation of sulphonamide compound in the retentate feed over

time due to permeation of water to permeate caused the foulant layer to build up on the surface of the membrane. This in turn will resulted in the increasing of water resistance at the membrane surface causing the water flux to decrease (Mahlangu et al., 2014).

Table 4.4: Comparison on final value of normalized fluxes of nanofiltration for four sulphonamide derivatives after 120 hours of experiment.

Compound	Normalized Flux		
	pH 5.6	pH 7.2	pH 10.0
SNM	0.8125 ± 0.04	0.7933 ± 0.02	0.8085 ± 0.03
SDZ	0.7155 ± 0.03	0.7278 ± 0.4	0.7181 ± 0.01
SMX	0.8045 ± 0.04	0.8061 ± 0.07	0.7952 ± 0.04
SDM	0.7308 ± 0.01	0.7270 ± 0.04	0.7340 ± 0.02

In addition, there is no significant changes observed in fluxes between all the three pH studied for sulphonamide derivatives. Apparently, pH of the solution did not play significant role in the rejection of sulphonamide using TS80 nanofiltration membrane. Similar observation was also found by Wang & Tang (2011) where only a slight difference in fluxes observed at pH 5.8 and 7.0. Since these pH value are higher than the isoelectric point of the membrane, which for this membrane is at pH 4 to 5, all the membrane exhibits the same negative charges, thus no obvious flux differences was detected between the pH tested.

Since pH only affect the reaction rate between free active chlorine and sulphonamide but did not significantly affect the rejection of sulphonamide, one pH value which is pH 7.2 was deemed sufficient for the study. pH 7.2 was decided based on the distribution of chlorine speciation where both hypochlorous acid and hyprochlorite ion exists in near equal amounts.

4.4 Combination of Chlorination and Nanofiltration for Sulphonamide Removal.

The central treatment is based on nanofiltration. A hybrid system is proposed which involves chlorination. The chlorination stage is combined with nanofiltration in three (3) different modes.

i. Chlorination followed by nanofiltration (Pre-chlorination)
ii. Simultaneous chlorination and nanofiltration (Simultaneous)
iii. Chlorination after nanofiltration (Post-chlorination)

The removal performance of sulphonamide, sulphonamide by-products and permeate fluxes for each system were discussed separately in this section.

4.4.1 Chlorination followed by Nanofiltration (Pre-chlorination)

4.4.1.1 Performance on removal of sulphonamide

In the pre-chlorination system, FAC was reacted with sulphonamide prior to the nanofiltration process. Two different concentrations of chlorine were added where one concentration was in excess (3.0 mg/L) while the other one was in limited quantity (0.75 mg/L). The performances on removal of four studied sulphonamide for pre-chlorination system in both limited and excess FAC were summarized in Figure 4.9 and Figure 4.10, respectively.

The rejection of 45.1%, 68.8%, 77.43%, and 92.86% were observed for SNM, SDZ, SMX and SDM, in limited FAC respectively. SNM with the smallest molecular weight (172 g/mol) had the lowest rejection among the tested sulphonamides followed by SDZ, SMX and then SDM being the highest rejection rate. Basically, the rejection for pre-chlorination system in limited FAC showed similar observation with the rejection of

sulphonamide using nanofiltration membrane only. However, from the observation on concentration of sulphonamide detected in permeate, the rejection is increased significantly for SNM and SDM (increased up to 28%) and increased slightly for SDZ and SMX. Limited chlorine added to the solution only helped by partially reacting with sulphonamide and thus reducing small concentration of sulphonamide in membrane feed whereby the nanofiltration membrane takes over the process next and that is why the rejection showed the same pattern with the study on nanofiltration only.

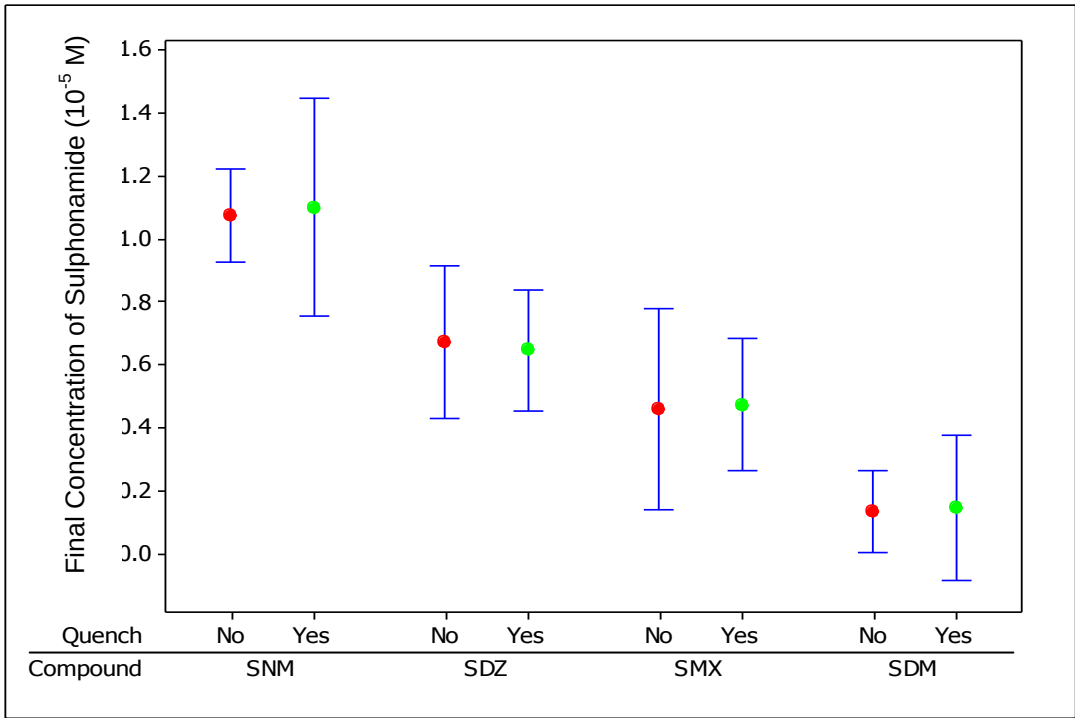


Figure 4.9: **Comparison on removal performance of sulphonamide in nanofiltration with and without quenching in the prechlorination system. ($[FAC]_0$ = 0.75 mg/L)**

As for the prechlorination system using excess chlorine, all the sulphonamide derivatives were reacted with excess chlorine, leaving only a trace amount of sulphonamide in the feed for the nanofiltration process. As result, significant removal of sulphonamide were achieved for this system where a complete removal was observed for SDM while there was approximately more than 99.35% rejection of the other tested

sulphonamides. Decreased concentration of sulphonamide in the pre-chlorination system feed water in general improved the overall rejection by nanofiltration.

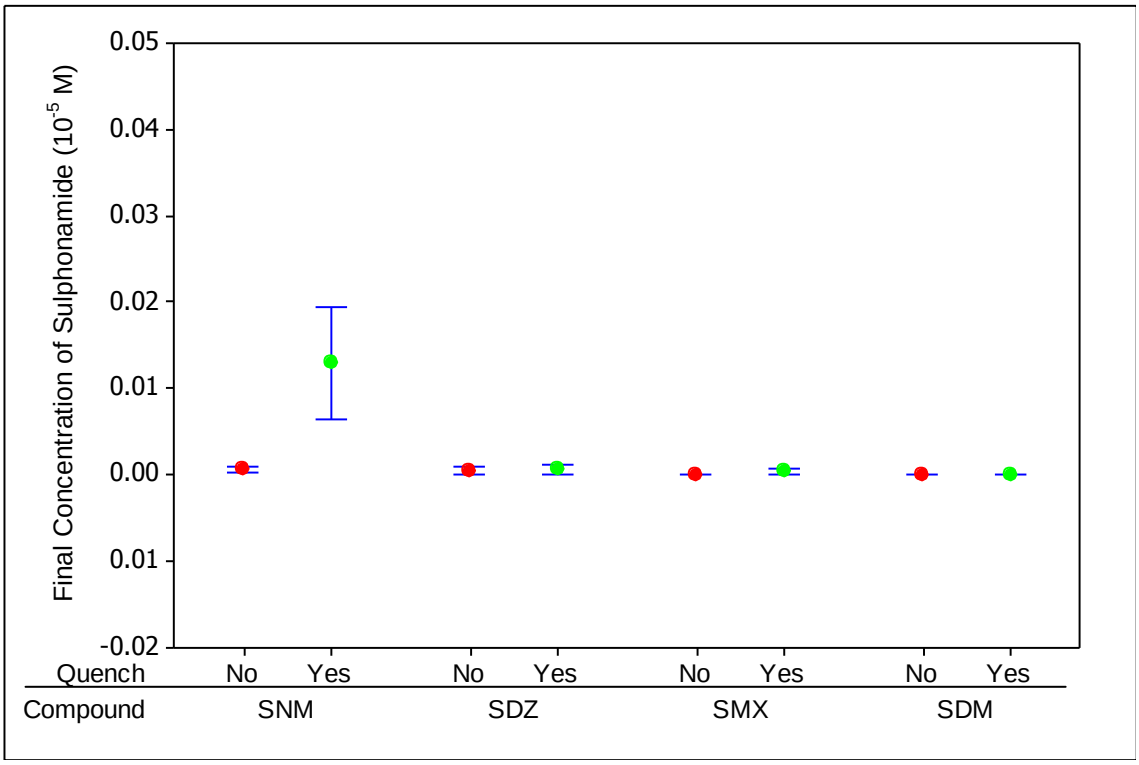


Figure 4.10: **Comparison on removal performance of sulphonamide in nanofiltration with and without quenching in the prechlorination system. ($[FAC]_0$ = 3.0 mg/L)**

However, it is noticeable that the concentration of sulphonamide in both limited and excess FAC increased after the dechlorination process. This occurred because some of the N-chlorinated sulphonamide managed to passed through into the permeate during the nanofiltration process and were successfully retransform to parent compound upon dechlorination. Nevertheless, the concentration of sulphonamide after dechlorination for limited FAC only increase slightly as oppose to the observation on section 4.4.3.1 where the concentration of sulphonamide increased significantly after dechlorination. This was due to the nanofiltration membranes' ability to reject most of the intermediate by-product (N-chlorinated sulphonamide) from passing through into the permeate and prevented the retransformation process from occurring on the permeate side.

4.4.1.2 Performance on removal of reaction by-products

Concentrations of major reaction by-products were monitored for both concentration of chlorine in the final effluent, and the results are shown in Figure 4.11. All of the by-products detected from the analysis were represented by their respective m/z ratio and peak area obtained from direct correlation between LC-TOF-MS and HPLC analysis.

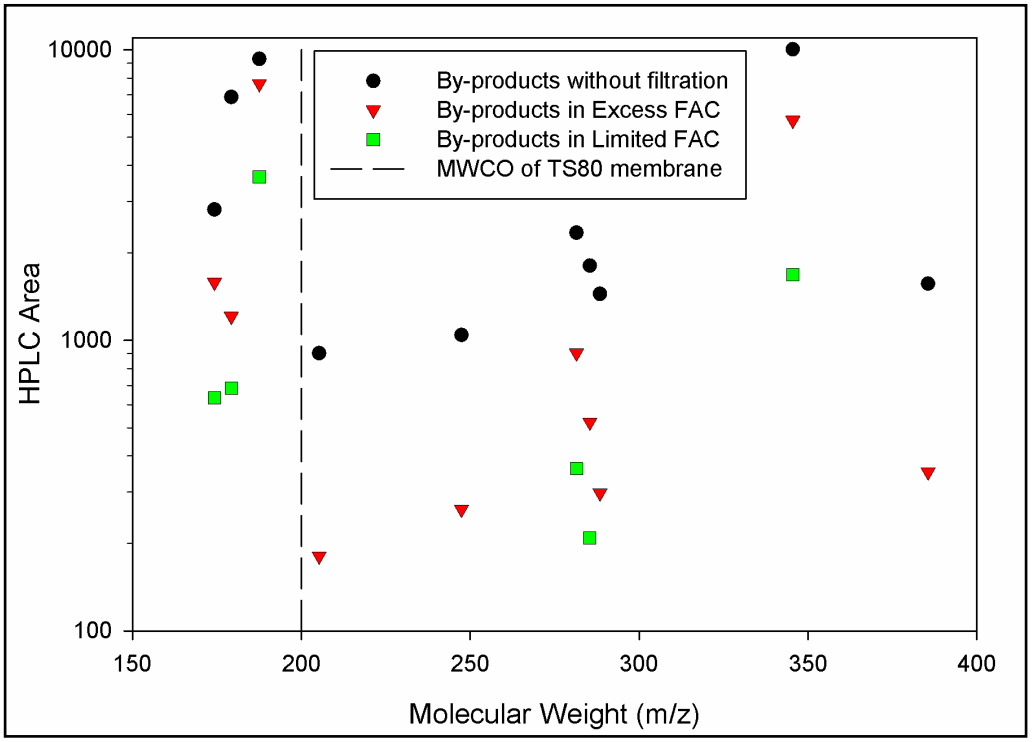


Figure 4.11: **Concentration of major by-products of four sulphonamide derivatives in prechlorination system for both limited and excess FAC prior to dechlorination process.**

The concentration of sulphonamide by-products in permeate were observed to be significantly reduced compared to concentration of by-products without nanofiltration process. Up to 73% of by-products formed during chlorination were successfully removed by nanofiltration and some of the major by-product for limited FAC system is not detectable by HPLC due to very low in concentration. Furthermore, higher concentration of sulphonamide by-products was observed in excess FAC system compared to limited FAC system. This is because excess FAC produce more by-

products in membrane feed compared to limited FAC when reacted with the same amount of sulphonamide thus resulted in more by-products that able to passed through into permeate.

In addition, concentration of N-chlorinated sulphonamide with molecular weight of 207.4, 285.4, 288.4, and 346.5 g/mol for SNM, SDZ, SMX, and SDM, respectively were considerably reduced and this resulted in only minor changes to the final concentration of sulphonamide after dechlorination. Evidently, nanofiltration membrane is effective in rejecting sulphonamide by-product formed during chlorination process.

Based on the observation found on the rejection of sulphonamide by-products, the rejection is mainly dominated by the size exclusion mechanism where by-product with molecular weight smaller than 200 g/mol were found to be higher in concentration in the permeate side compared to by-product that bigger than 200 g/mol. This is due to the inability of the nanofiltration membrane to effectively reject particles smaller than the membrane MWCO (200 Da).

4.4.1.3 Normalized flux

To study the effect of pre-chlorination system to the fluxes, membrane filtration were run in batches for a few times until a total of 120 hours operational time is achieved. The final fluxes reading were obtained and plotted into Figure 4.12.

We can see that the pre-chlorination system significantly improves the permeate flux compared to the flux for nanofiltration only. After a total of 120 hours' worth of batch nanofiltration processes at 5 bar pressure, nanofiltration membranes in pre-chlorination

system showed a substantial increase in the normalized fluxes in both applied concentration of FAC. This is possible due to the reduced concentration of sulphonamide in the membrane feed from the reaction with FAC. A reduced foulant in membrane feed (which in this case is sulphonamide) will lower the chances for the membrane to foul from the pore blockage on the surface by the foulant (Sadmani et al., 2014). Continuous exposure of chlorine to the membrane surface also contributes to the increase of permeates fluxes by partially cleaning the membrane surface since chlorine also can act as membrane cleaning agent (Kang, et al., 2007). Further explanation on the effect of chlorine to the flux changes, membrane stability and morphology will be discussed in section 4.5.

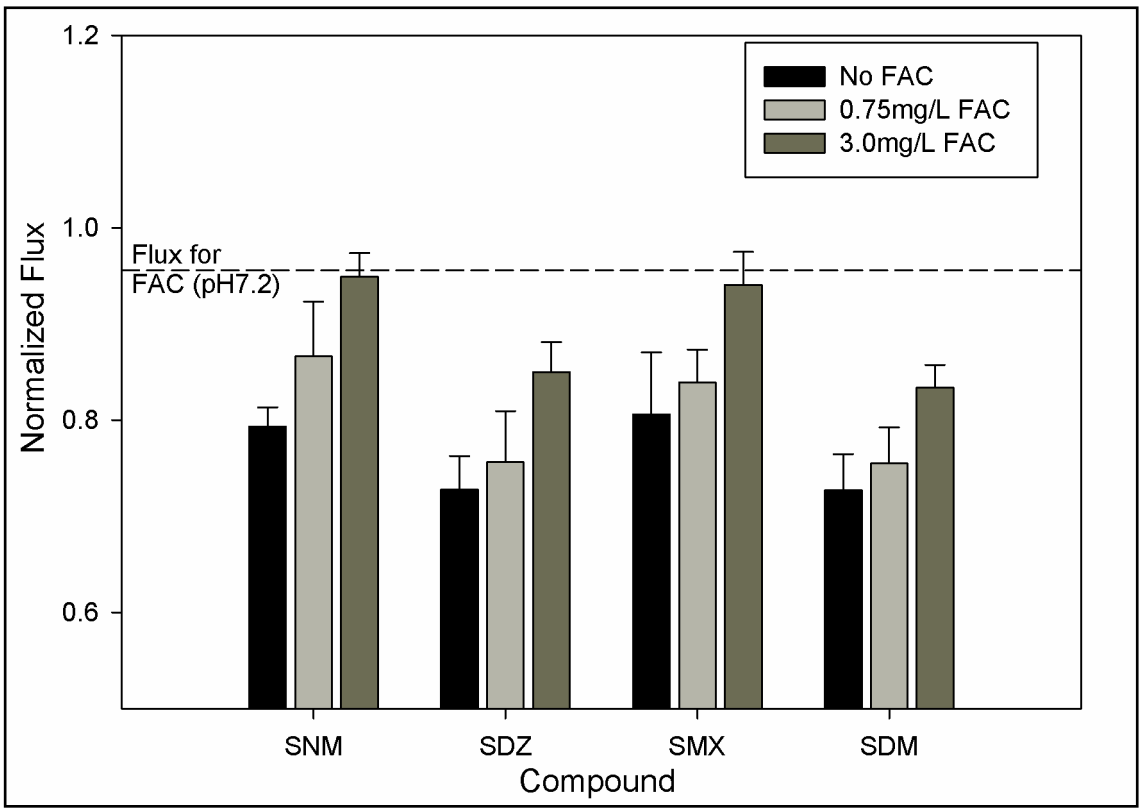


Figure 4.12: **Comparison on relative fluxes between different concentrations of FAC used in prechlorination system after 120 hours of experiments.**

Furthermore, it is also observed that at low concentrations of FAC (0.75 mg/L), the changes on fluxes were barely noticeable compared to the fluxes for high concentration

of FAC (3.0 mg/L). It is understandable that the flux for limited chlorine is lower compared to when excess chlorine was added due to inability of limited chlorine to fully react with excess sulphonamide. Sulphonamide residual that are not reacted with FAC would accumulate on the retentate over time and thus resulted in the flux reduction.

4.4.2 Simultaneous Chlorination and Nanofiltration

4.4.2.1 Performance on removal of sulphonamide

In the simultaneous system, chlorination and nanofiltration process was conducted concurrently. Two mg/L FAC was spiked into the membrane feed every 1 hour continuously for 14 hours of filtration and at the next 10 hours of filtration, no chlorine dosage were given to the membrane feed. After that, the procedure is repeated until a total of 120 hours of filtration was achieved. The purpose of the termination of chlorine doses for 10 hours after every 14 hours of filtration is to observe on what would happen when there is no chlorine in the system. A constant concentration of sulphonamide was fed into the membrane feed in order to maintain the working volume of the system.

The removal of sulphonamide in simultaneous chlorination and nanofiltration was shown in Figure 4.13. During the first 14 hours of the system, near complete removal was observed for all sulphonamides. Like pre-chlorination system, excess chlorine in membrane feed caused the concentration of sulphonamide to decrease significantly. As a result, only a very small amount of sulphonamides ($< 1x\ 10^{-9}$ M) were successfully passed through the membrane after nanofiltration. Ignoring the observation on sulphonamide concentration after chlorine termination, simultaneous system was found to be effective in removing sulphonamide.

It was found that the sulphonamide in the permeate increased rapidly especially for SNM up to $4.8x10^{-6}$ M after 10 hours of chlorine termination. The increase of sulphonamide concentration in membrane feed due to the continuous feed of sulphonamide solution together with the depletion of chlorine in the feed caused the accumulation of sulphonamide in membrane feed and like a normal nanofiltration process, part of the sulphonamide will move into the permeate through the membrane causing the increases of sulphonamide reading on permeate side after a few hours.

Another interesting observation was found after chlorine was added after that. Concentration of sulphonamide in the permeate were found to decreased rapidly until the concentration reach to almost zero after the chlorine dosage started. It is appear that the chlorine added to the feed of the nanofiltration system passed through into the permeate and reacted with the residual sulphonamide present in permeate thus decreasing the sulphonamide concentration rapidly. This finding was proven by the detection of chlorine residual (up to 0.4 mg/L) in the permeate side from the analysis of every 800 mL permeate. Similar finding was found by Gu et al. (2012) where 27–28% permeability of HOCl, a species of chlorine was observed in permeate. Low molecular weight together with the neutral charge of HOCl attributed to the easy diffusion of the HOCl into the permeate (Gu, et al., 2012). This is also one of the reasons on why the concentration of sulphonamide in simultaneous system after chlorine termination were lower in the permeate compared to the concentration observed on nanofiltration only. Sulphonamide is not only reacted with residual chlorine on retentate side but also on permeate side thus resulted in low final concentration of sulphonamide in permeate.

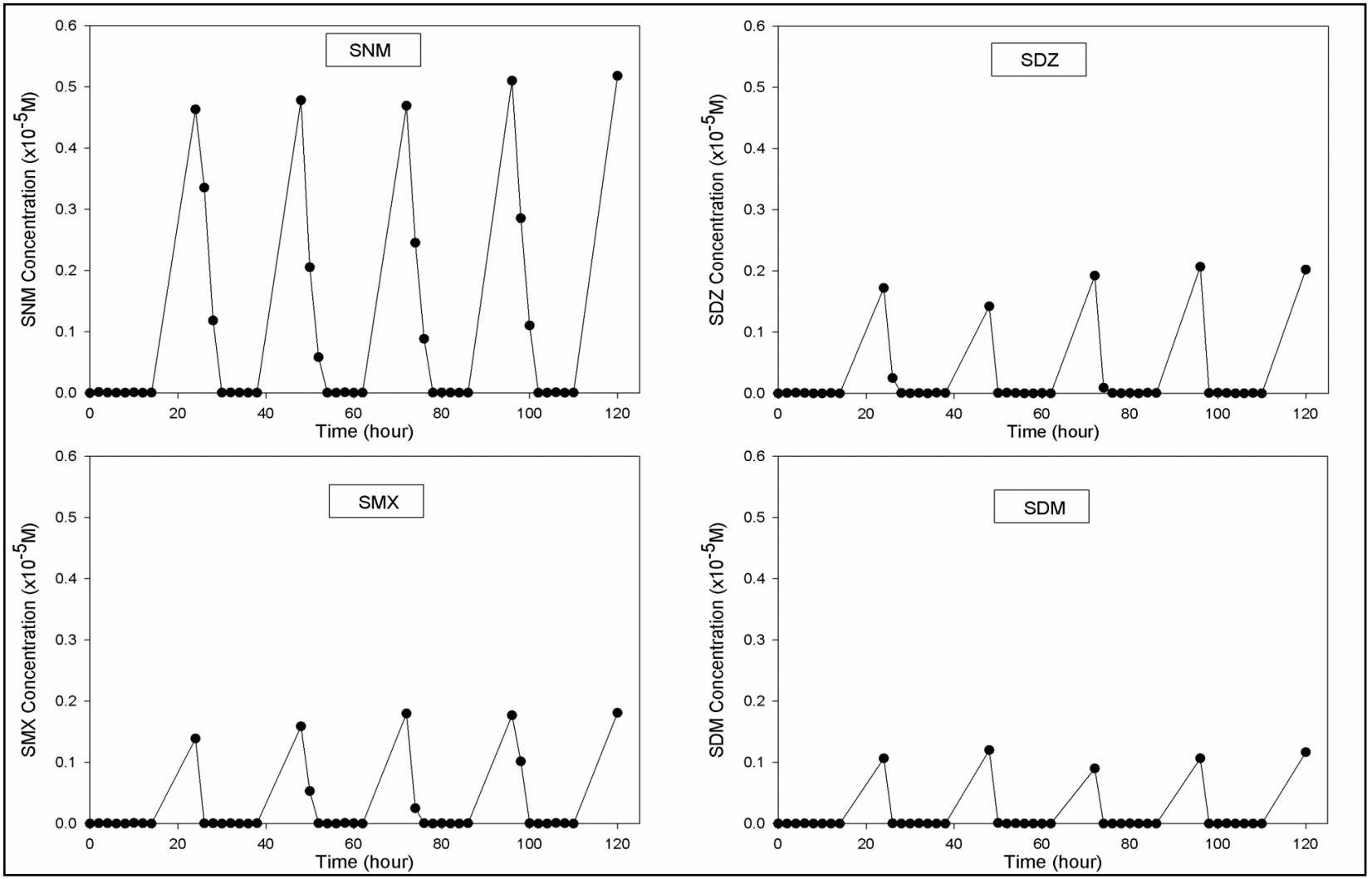


Figure 4.13: **Comparison on overall removal performance of sulphonamide derivatives in simultaneous system.**

4.4.2.2 Performance on removal of reaction by-products

The concentration of sulphonamide by-products in final effluent of both concentration of FAC were observed to be significantly reduced compared to concentration of by-products without filtration process. From Figure 4.14, a significant removal of sulphonamide by-products was observed, with more than 82% of the major by-products was successfully removed by simultaneous system. This is similar in pattern with the rejection of by-products observed for pre-chlorination system where larger molecular weight of by-products (> 200 m/z) is rejected more than the low molecular weight by-products (< 200 m/z). This is because the rejection of sulphonamide by-product is dominated by the size exclusion mechanism where higher molecular weight compound will be rejected more compared to low molecular weight compound. For compound with molecular weight lower than molecular weight cut off(MWCO) of the membrane (200 Da), electrostatic repulsion acts as a major rejection mechanism since at pH7.2, most of the sulphonamide by-products are negatively charged (García-Galán, et al., 2008).

In addition, concentration of N-chlorinated sulphonamide intermediate by-products with molecular weight of 207.4, 285.4, 288.4, and 346.5 g/mol for SNM, SDZ, SMX, and SDM, respectively were found to be very low in final effluent due to the excessive reaction of chlorine with the intermediate by-products in either retentate side or permeate side that will further transform said compound into other final by-products.

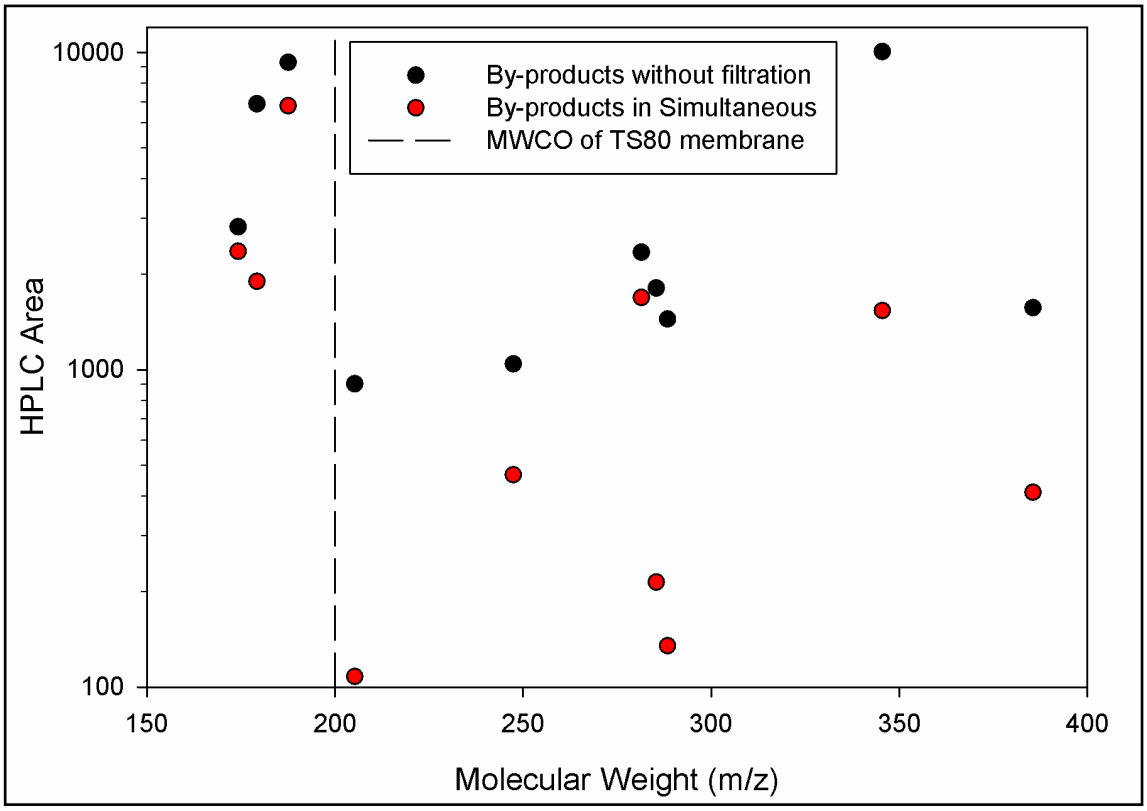


Figure 4.14: **Concentration of major by-products of four sulphonamide derivatives in permeate side of simultaneous system prior to dechlorination process.**

4.4.2.3 Normalized flux

From Figure 4.15, we can see that the flux for all sulphonamide derivatives in simultaneous are steadily increase throughout the experiments. At the final 120 hours of filtration, 10.48% increase of flux was observed for SNM while 4.04% and 8.62% were observed for SDZ and SMX, respectively. A slight decrease however was detected for flux of SDM with 1.59% decrease after 120 hours. A reaction of sulphonamide with FAC resulted in lower amount of sulphonamide concentration in the membrane feed and in turns will have a higher flux compared to the flux for nanofiltration of sulphonamide without chlorination.

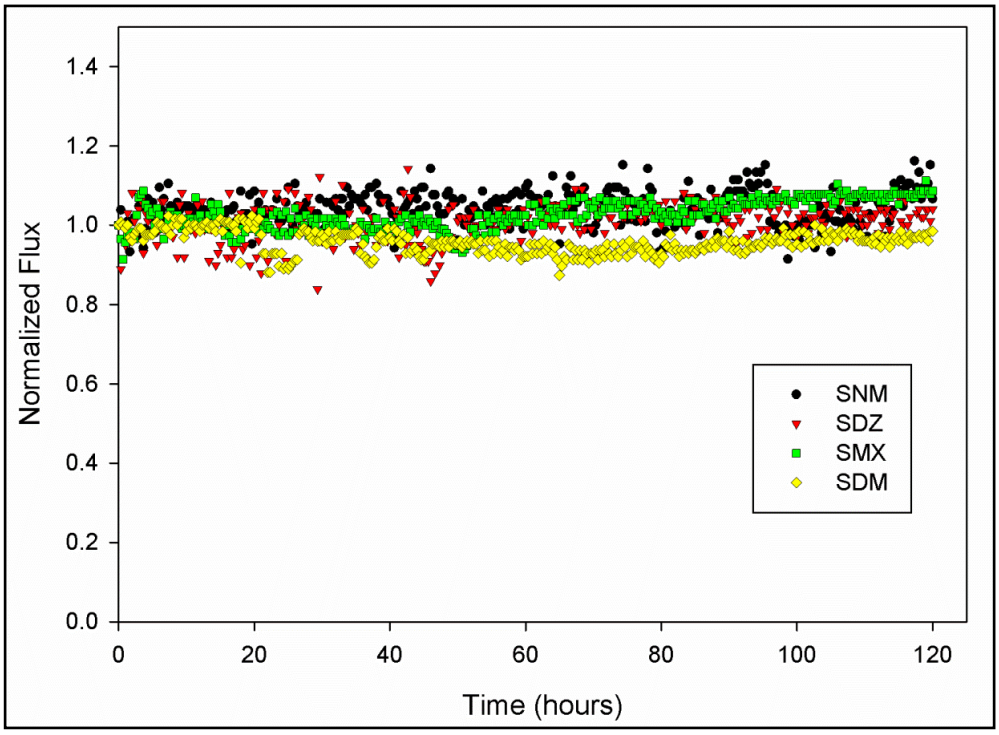


Figure 4.15: **Comparison on relative fluxes between sulphonamide derivatives in simultaneous system.**

A slight decrease of fluxes was also detected for all sulphonamides after ~20 hours of filtration. First termination of the chlorine dosage at 14 hours of filtration caused the sulphonamide to accumulate slowly over time in retentate side and caused the membrane flux to decrease slowly up until the next chlorination session (at hour 24) where the flux start to increase again to original value.

However, continuous increases of membrane flux over time that is more than the flux value of ultrapure water (value of 1) suggests that the membrane degradation took place from the continuous dosage of excess FAC oxidant to the surface of the membrane (Kang, et al., 2007). This is due to the limitation of composite polyamide membrane in which according to the specification given by the manufacturer, the maximum concentration of FAC that the TS80 membrane can tolerate continuously is 1ppm. Any higher than that would weaken the polyamide bond on the surface of the membrane and as a result a pore size will increase and thus increase flux rate (Kang, et al., 2007; Xu et al., 2013). In this case, more than 1ppm of residual chlorine were left on

the membrane feed after chlorination and continue to increase over time as more chlorine is added every hour. Further discussion on the effect of residual chlorine to the fluxes of membrane is discussed in section 4.5.3.

4.4.3 Nanofiltration followed by Chlorination (post-chlorination)

4.4.3.1 Performance on removal of sulphonamide

In the post-chlorination system, FAC was reacted for at least 30 minutes of contact time with permeate of sulphonamide collected from the nanofiltration study in section 3.3. The same concentrations of FAC used in pre-chlorination system (0.75 mg/L for limited and 3.0 mg/L for excess FAC) was applied to the permeate solution. Figure 4.16 and Figure 4.17 summarizes the performance of post-chlorination system for both limited and excess FAC in terms of total sulphonamide removal for the four studied compounds.

In excess FAC, all sulphonamides derivatives were observed to almost reach zero concentration. Up to 99.96% of sulphonamides were successfully removed using post-chlorination system. Comparison with chlorination of sulphonamide without nanofiltration also showed similar results. In this case, nanofiltration might be unnecessary for the removal of sulphonamide except for the removal of reaction by-products only which will be explain in the next section.

Significant removal of sulphonamide derivatives were also detected in limited FAC system where 67% of SNM was removed while more than 95% removal were observed for other three sulphonamide. With the nanofiltration process alone that removes up to

79% of sulphonamide, only a small concentration of sulphonamide is left in permeate for chlorination.

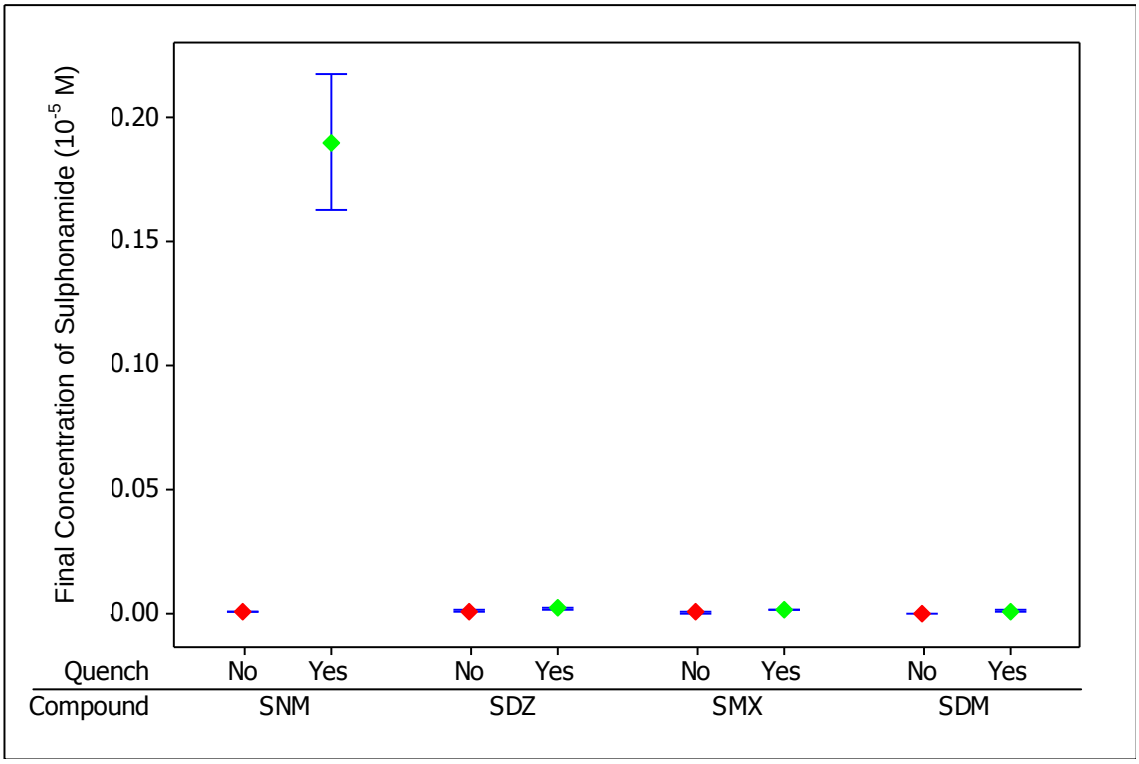


Figure 4.16: **Comparison on overall removal performance of sulphonamide in nanofiltration with and without quenching in the post-chlorination system. ([FAC]0 = 3.0 mg/L)**

However, it was also observed that the concentration of sulphonamide increased especially for SNM after the quenching process. More than 52% of SNM was found to be increased while the other sulphonamide compound increased up to 19% in limited FAC. The same phenomenon also occurred to the sulphonamide when excess FAC was used, although the concentration only increased slightly compared to when limited FAC was used. This is due to the amount of N-chlorinated sulphonamides which is able to retransform to their respective parent compound that is high in the final effluent. The lack of filtration system after the chlorination process resulted in the considerably high amount of intermediate by-products which in turns increased the final concentration of sulphonamide after quenching.

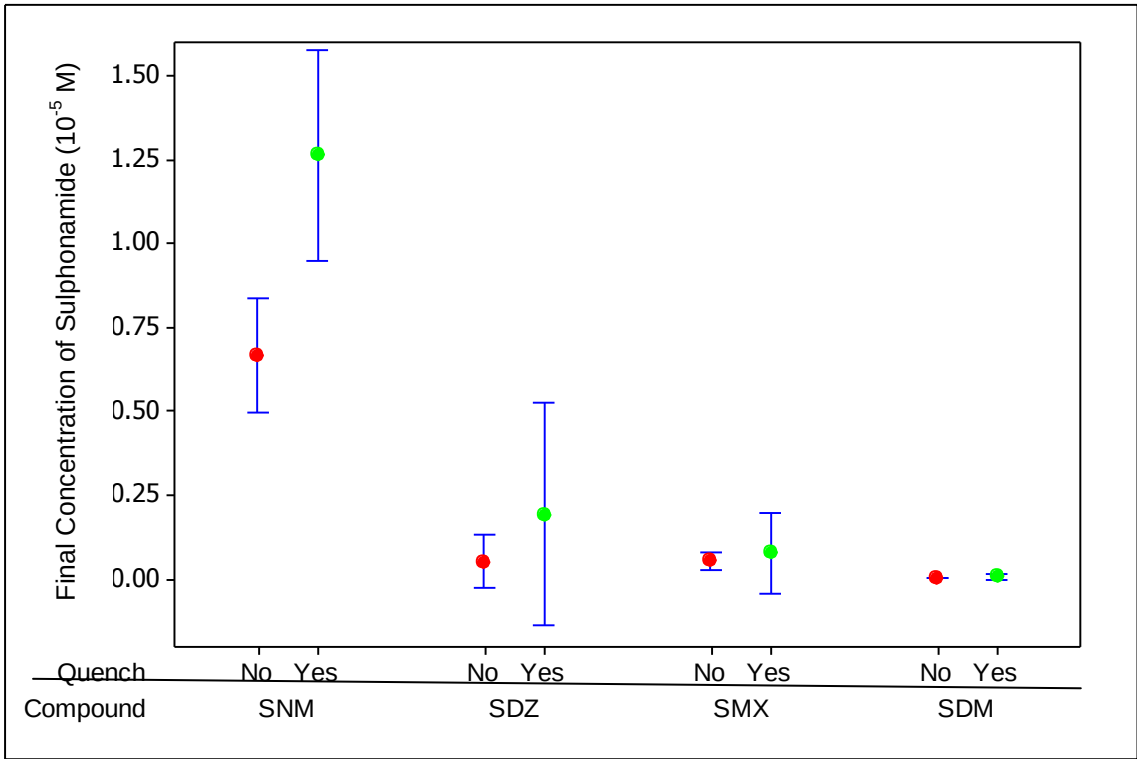


Figure 4.17: **Comparison on overall removal performance of sulphonamide in nanofiltration with and without quenching in the post-chlorination system. ($[FAC]_0$ = 0.75 mg/L)**

4.4.3.2 Performance on removal of reaction by-products

Concentrations of major reaction by-products in both limited and excess FAC were detected in the final effluent of post-chlorination system and the results are shown in Figure 4.18.

The concentration of sulphonamide by-products in final effluent of both concentration of FAC were observed to be significantly reduced compared to concentration of by-products without filtration process. Up to 90% of by-products formed during chlorination were successfully removed by post-chlorination system. Low residual sulphonamide in the permeate due to nanofiltration process resulted in low concentrations of reaction by-products detected in post-chlorination system after chlorination process. Furthermore, higher concentration of sulphonamide by-products

was observed in excess FAC system compared to limited FAC system. This is because limited chlorine can only reacted with finite amount of residual sulphonamide present in the permeate of nanofiltration whereby excess chlorine can react with the whole residual sulphonamide in permeate and produced more final by-products.

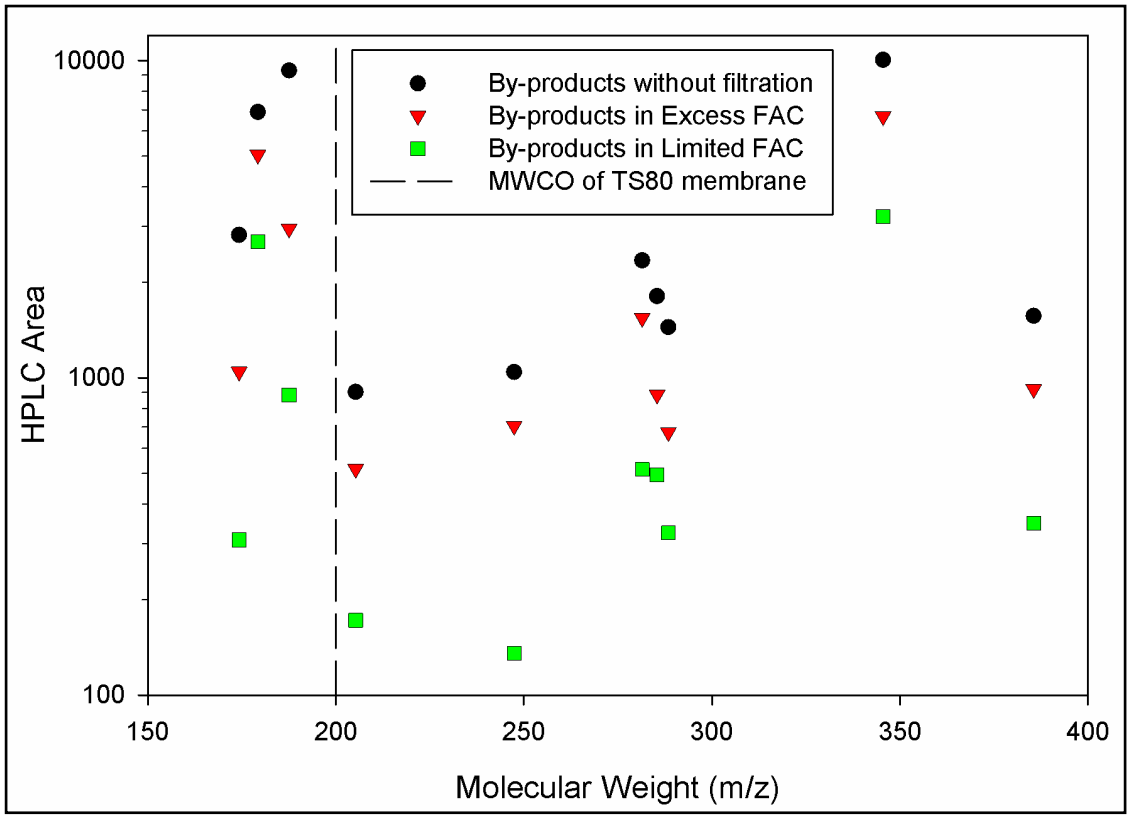


Figure 4.18: **Concentration of major by-products of four sulphonamide derivatives in post-chlorination system for both limited and excess FAC prior to dechlorination.**

However, the concentration detected for N-chlorinated sulphonamide is considerably high and this resulted in major changes to the final concentration of sulphonamide after dechlorination process especially for system with limited FAC. N-chlorinated sulphonamide is an intermediate by-product that able to retransform to parent compound with molecular weight of 207.4, 285.4, 288.4, and 346.5 g/mol for SNM, SDZ, SMX, and SDM, respectively.

4.4.3.3 Relative flux

Since post-chlorination system uses permeate feed from nanofiltration studied in section 3.3, the reading on flux is exactly the same as in the discussion at section 4.3.2 where the relative fluxes for all sulphonamide derivatives decreased slightly after 24 hours of experiments due to the accumulation of sulphonamide compound on the retentate feed.

4.5 Comparison on the Overall Effectiveness between Various Systems.

4.5.1 Rejection of sulphonamide

Since the simultaneous system in this study was run in continuous mode as compared to pre-nanofiltration system where the process were run in batches, certain rules have to be set so that the comparison can be made between these two systems. In this case, all the results obtained at permeate volume of 800 mL for both systems were used for comparison. For pre-nanofiltration system, results obtained at FAC concentration 3.0 mg/L (excess FAC) was used for comparison instead of 0.75 mg/L (limited FAC) since the simultaneous system also was conducted using excess FAC.

The comparison was made using quenched samples where there is no FAC residual present in the final effluent so that the effectiveness of membrane filtration in removing total sulphonamide could be determined. Furthermore, in excess volume of FAC, the amount of sulphonamide intermediate by-products that are able to retransform to their respective parent compound are very small in quantity (< 1%) and will not affect the measurement of final concentration of sulphonamide, as discussed in section 4.2.2.

Based on comparison results on Table 4.5, the rejection rates for all sulphonamide derivatives in all the systems studied were almost complete removal. However, in the post-nanofiltration system, the rejection rate of sulfanilamide (SNM) was way below (88.31% rejection only) compared to the other hybrid systems.

Table 4.5: **Comparison on the rejection rate of total sulphonamide in different systems studied.**

Rejection Rate (%)			
Comp.	Pre-chlorination System	Simultaneous System	Post-chlorination System
SNM	99.35	99.87	88.31
SDZ	99.97	99.96	99.91
SMX	99.98	99.98	99.93
SDM	100.00	100.00	99.96

As mentioned before in the section 4.4.1.1 and section 4.4.3.1, the differences in removal efficiencies between the post-nanofiltration and the other two systems was because of some of the N-chlorinated sulphonamide produced during the chlorination process of sulphonamide that managed to passed through into the permeate during the nanofiltration process and were successfully retransform to parent compound upon quenching process. Sulfanilamide (SNM) is the most affected from this phenomenon due to its small molecular size of N-chlorinated SNM by-product (206 g/mol) compared to membranes' molecular weight cutoff (200 Da) that caused the by-product to pass through during nanofiltration.

However, an interesting phenomenon was observed when limited concentration of FAC was used. At low concentration of FAC ([sulphonamide]: [FAC] >1), it was shown that the removal of sulphonamide in the pre-chlorination system was lower compared to

post-chlorination. This is contrary to the results obtained when excess FAC was used. With the nanofiltration process alone that removes up to 79% of sulphonamide, only a small concentration of sulphonamide is left in permeate. Further chlorination of permeate could only result in an excess of FAC and thus N-chlorinated sulphonamide will further react into another compound. However, slightly lower removal of SNM was achieved in the post-chlorination system compared to the pre-chlorination system, due to the inability of the nanofiltration membrane to reject lower molecular weight compounds than the membrane MWCO; thus a higher concentration of SNM would be present in permeate.

Overall, pre-nanofiltration and simultaneous hybrid system showed the best removal efficiencies of sulphonamide derivatives compared to post-nanofiltration systems. On another note, filtration of a mixture of all sulphonamides together in one feed solution does not give noticeable change in removal efficiency compared to individual filtration. This suggests that low or no interaction occurred between those compounds and their by-products that could significantly affect the performance of the membrane.

4.5.2 Rejection of sulphonamide by-products

The ability of nanofiltration membranes in removing reaction by-products is also a matter of concern, due to the acute characteristic of some reaction by-products (García-Galán et al. 2008). For example, study by Dantas, et al. (2008) on the acute toxicity of by-product formed during ozonation process of sulphonamide showed that sulfamethoxazole (SMX) intermediate by-product formed in the first 30 minutes has higher toxicity compared to untreated SMX so it is deemed compulsory to study the rejection of by-products of sulphonamide during nanofiltration. Comparison of major reaction by-products concentrations in the permeates between all the hybrid systems are

shown in Figure 4.19. Since identification of the reaction by-products was not covered in this study, all of the by-products detected from analysis were represented by their respective m/z ratio and HPLC peak area obtained from direct correlation between LC-TOF-MS and HPLC analysis.

The same case used in comparison between the hybrid systems for rejection of sulphonamide was also applied for the comparison in rejection of its by-products except the results taken are from the unquenched samples. This was done in order to preserve the intermediate by-products from retransform so that the effectiveness of membrane in rejecting these compounds could be determined.

There was no clear pattern on the rejection rate between these three systems as the concentration of each by-products detected were close to each other. However, it was noticeable that all the compounds in the post-nanofiltration system that is higher than 200 m/z molecular weight showed the highest concentration detected in the permeate compared to the other systems. High residual of sulphonamide concentration after nanofiltration process in the post-nanofiltration system resulted in higher concentration of by-products produced after the chlorination process.

There were some of the compounds especially for compounds with low molecular weight (below 200 g/mol) in pre-nanofiltration and simultaneous systems that showed higher concentration detected in the permeate compared to post-nanofiltration system. This is because of the inability of the nanofiltration membrane to reject particles smaller than the membrane pore size (200 Da).

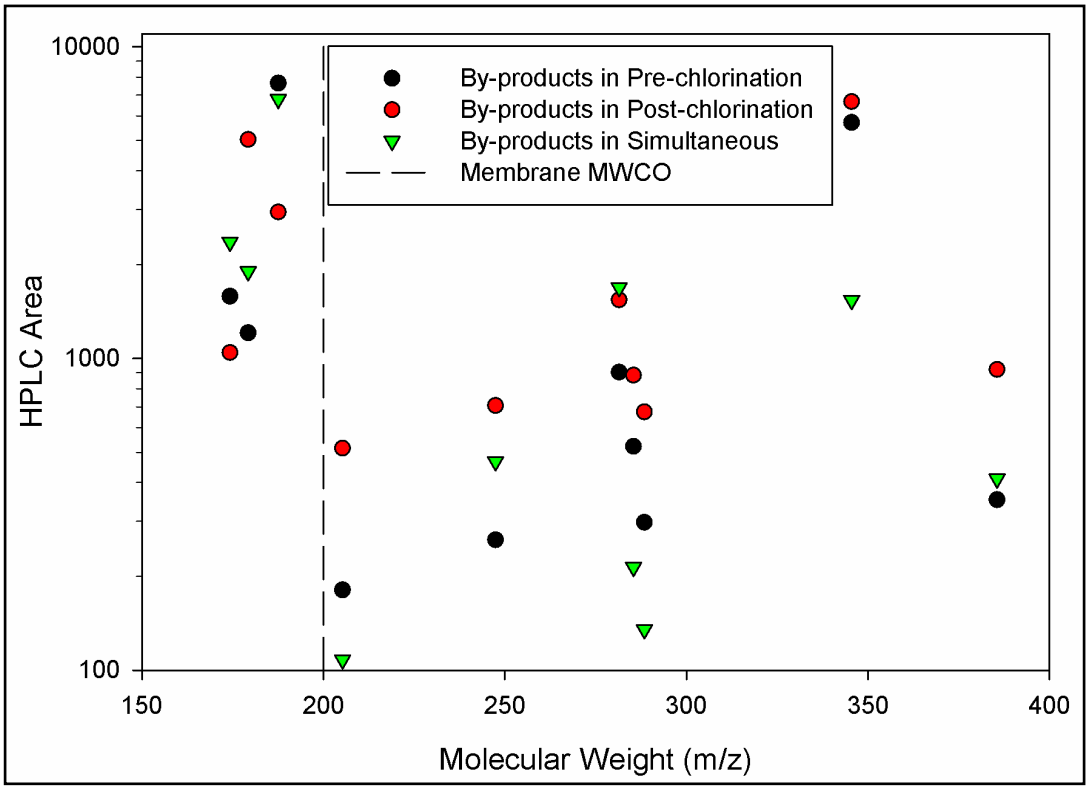


Figure 4.19: **Comparison of major reaction by-products concentrations based on the molecular weight ion fraction (m/z) in the permeates between all the hybrid systems prior to quenching process.**

Comparison between pre-nanofiltration system and simultaneous system showed that the concentration of N-chlorinated sulphonamide which is 207 m/z, 285 m/z, 288 m/z and 345 m/z for SNM, SDZ, SMX, and SDM, respectively for simultaneous system is lower compared to pre-nanofiltration system. The excess FAC presence in permeate caused the N-chlorinated sulphonamide to further reacted to another compound thus reducing its concentration. This was due to the FAC that passed through into permeate from continuous dosage of FAC in the membrane feed.

Since sieving mechanism which involves molecular size is not the only factor that determines the rejection efficiencies, other factors such as charge repulsion and adsorption need to be taken into consideration. Different surface charge between each by-product might contribute to the differences in by-products concentration found in permeate (Comerton, et al., 2007; Kallioinen & Nyström, 2008). Further study on the

characteristic of the by-products might be needed in order to accurately determine the effect of adsorption and surface charge of by-products that occurs during the nanofiltration. Overall, simultaneous system showed the best removal efficiencies of sulphonamide reaction by-products compared to the other systems studied.

4.5.3 Relative flux

From the Figure 4.20, we can see that the pre-chlorination and simultaneous systems significantly improves the permeate flux compared to the post-chlorination system. Note that the flux for post-chlorination is the data collected from flux for nanofiltration only since in the post-chlorination system, permeates from nanofiltration is used for chlorination.

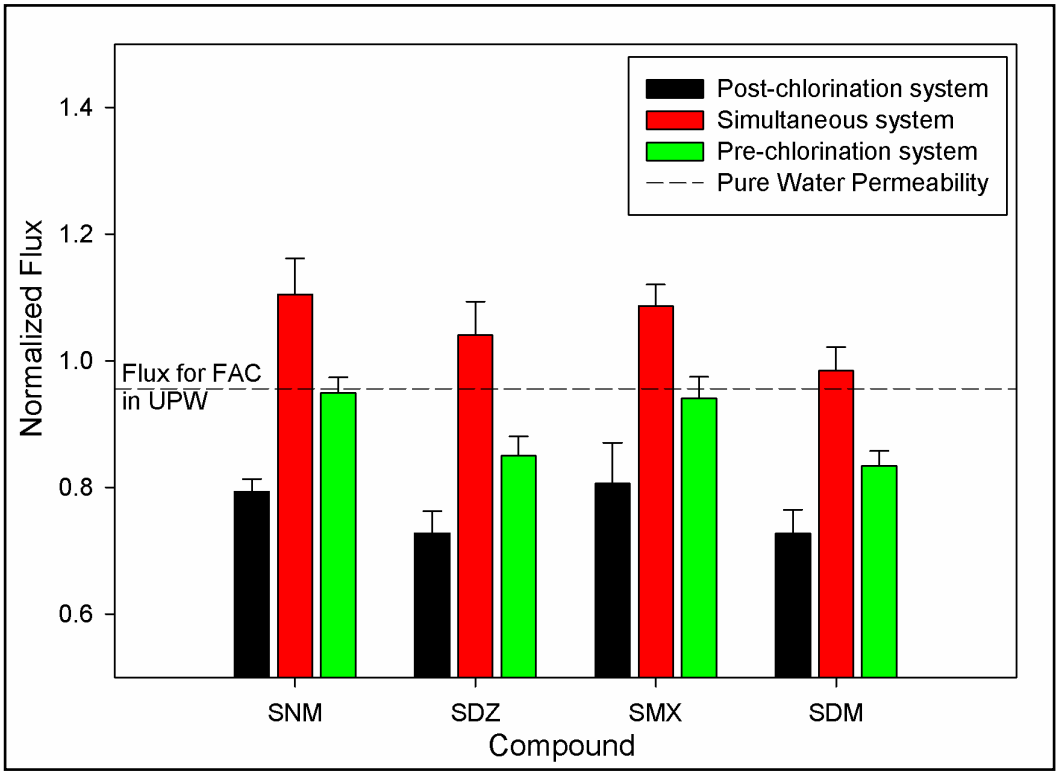


Figure 4.20: **Comparison on relative fluxes between all three systems studied after 120 hours of experiments.**

Overall, a reduced concentration of sulphonamide in the membrane feed due to reaction with FAC, combined with continuous exposure of the membrane to chlorine,

contributed to the increase of permeates fluxes. The presence of residual chlorine in the membrane feed cleans the surface of the partially fouled membrane thus increases the fluxes (Kang, et al., 2007). However, prolonged exposure to chlorine could introduce irreversible damage to the membrane, due to polyamide degradation, which is the main factor that reduces the lifetime of nanofiltration membranes. To confirm this, nanofiltration of 3 mg/L(ppm) chlorine in ultrapure water were conducted at pH 7.2 for 120 hours and the results are shown in the same Figure 4.20.

The exposure of 3.0mg/L of chlorine to the membrane at pH 7.2 reduced the flux by ~5% after 120 hours. The decline in flux can be attributed to the deformations of polyamide chains by chlorine. At mild chlorination, the destruction of a polyamide rigid structure caused the changes of the polymer chain flexibility. Under pressurized nanofiltration, the polymer chains could be compacted thus causing the flux to decrease (Gu, et al., 2012; Kwon & Leckie, 2006). Alternatively, tightening effect caused by increased polyamide chains also contributed to the decrease of flux (Soice et al., 2003). The authors suggested that the tightening effect can occur at mild chlorination resulted from the formation of additional crosslinking via azocompounds at the surface of the membrane, causing it to be less permeable.

Expectedly, the flux for nanofiltration of chlorine in ultrapure water was higher than the flux of pre-chlorination system. The declines of fluxes from the tightening effect and increased hydrophobicity of the membrane outweight the benefit of reduced sulphonamide compound in feed from chlorination, together with mild cleaning of membrane surface by FAC. Furthermore, increased sulphonamide by-products in the feed also contributed to the reduction of flux in pre-chlorination system by acting as a

foulant which will block the pore size and accumulate on the membrane surface thus reducing the fluxes reading.

It was also found that the pH of the feed in pre-chlorination decreased over time to less than pH 5.0 after 24 hours of filtration due to the reduction of chlorine in the feed into permeates and also from the increases of acidic sulphonamide by-products in permeate feed. In acidic region, hypochlorous acid was dominant and its deleterious effect of the membrane is much more severe compared to at pH 7.2 (Do et al., 2012a; Mitrouli et al., 2010). These resulted in more degradation of polymer chain and also increase in the formation of additional crosslinking via azocompound, thus reducing higher flux value in pre-chlorination system upon compaction by pressure. By repeating the experiment in batches caused the membrane to be exposed at reduction of pH over time repeatedly (pH 7.2 to < pH 5.0 for both start and at the end of the experiment, respectively) and thus giving deleterious fluxes readings.

However, different observation was found on simultaneous system where the flux for simultaneous system was higher than the flux of nanofiltration of ultrapure water. Increases of membrane flux more than the flux value of ultrapure water suggests that the membrane degradation took place from the continuous dosage of excess FAC oxidant to the surface of the membrane. Continuous exposure of chlorine to the membrane over time will increase the pH of the membrane feed due to the accumulation of chlorine, which is alkaline, in the feed. At high pH, hydrogen bonds broke by the chlorine which caused the membrane to swell from all the repulsive interaction between groups of carboxylic acid inside the polymer chain. The chlorine that diffuses into the polymer chains will further break the hydrogen bonds and extend the swelling which will increase the segmental movement of the polymer chains. This in turn will reduce the

water passage restriction (pore size enlargement) through the membrane and resulted in the increase of flux higher than the flux for ultrapure water (Gu, et al., 2012; Kang, et al., 2007; Kwon & Leckie, 2006).

4.5.4 Salt Rejection

Polyamide membrane is known to be susceptible to oxidation processes, especially with chlorine. Because of that, rejection testing of standard salt was done as to find out whether membranes used in the pre-chlorination and simultaneous system were damaged or not from continuous exposure to residual FAC. Salt rejection efficiencies of membranes for both systems (after 120 hours of operation) were evaluated and compared. For the post-chlorination system where there was no FAC introduced into the membrane feed, ~93.6% of sodium chloride (NaCl) was successfully rejected. As for the pre-chlorination system, the rejection of sodium chloride using the membrane from the pre-chlorination system with limited FAC (0.75mg/L FAC) was lower with ~94.8% of rejection rate compared to using membrane from the pre-chlorination system with excess FAC system (3.0mg/L FAC) where ~94.3% of rejection was achieved. This suggests that the membranes used in the pre-chlorination systems were not heavily damaged and still exhibited the same removal capability compared to the nanofiltration membrane without chlorine exposure. Other study by Do et al. (2012b) also reported similar results where the salt rejections were increased in mild chlorination of the membrane. The increases of inorganic salt rejection were due to the combination of tightening effect and the enhanced membrane surface negativity caused by the hydrolysis of C-N bond, producing more –COOH group on the surface of the membrane which will repel the salt and increase the rejection.

However, the same cases did not apply to the hybrid system. The rejection rate of sodium chloride using the nanofiltration membrane used in hybrid system dropped from ~92.7% to ~90.92%. Again, this result suggests that the membrane degradation took place where the pore size is enlarging from the continuous dosage of excess FAC oxidant to the surface of the membrane (Gu, et al., 2012; Kwon & Leckie, 2006). Although the value did not drop significantly, but for long term continuous use, the rejection rate could drop until the membrane may become unusable.

Based on the observation of salt rejection, post-chlorination system showed the best membrane stability compared to the other two systems studied due to absence of chlorine in membrane feed of post-chlorination system.

4.5.5 FTIR Analysis

ATR-FTIR (BRUKER Tensor 27 FT-IR) was used to analyze the surface structure the membranes used in this experiment. The FTIR spectra of the changes in chemical structure are shown in Figure 4.21.

From the overall pattern, no significant changes were observed between membrane used in prechlorination and postchlorination. Although the concentration of chlorine used in this study (3.0 ppm) are a bit higher that the chlorine tolerance of the TS80 membrane (~1 ppm), no reduction or increases of intensity for amide bond (1540 cm^{-1}) and hydrogen bond (1608 cm^{-1}) were observed for all three membranes. This indicated that no significant damage occurred between chlorine and polyamide chains on the membrane surface for prechlorination system.

This is possibly due to the coating layer that covers the surface area of the membrane containing the polyamide active sites (Xu, et al., 2013). Residual chlorine left from the reaction of sulphonamide may not be able to damage the membrane's surface characteristic, thus no changes found on chemical structure of the membranes.

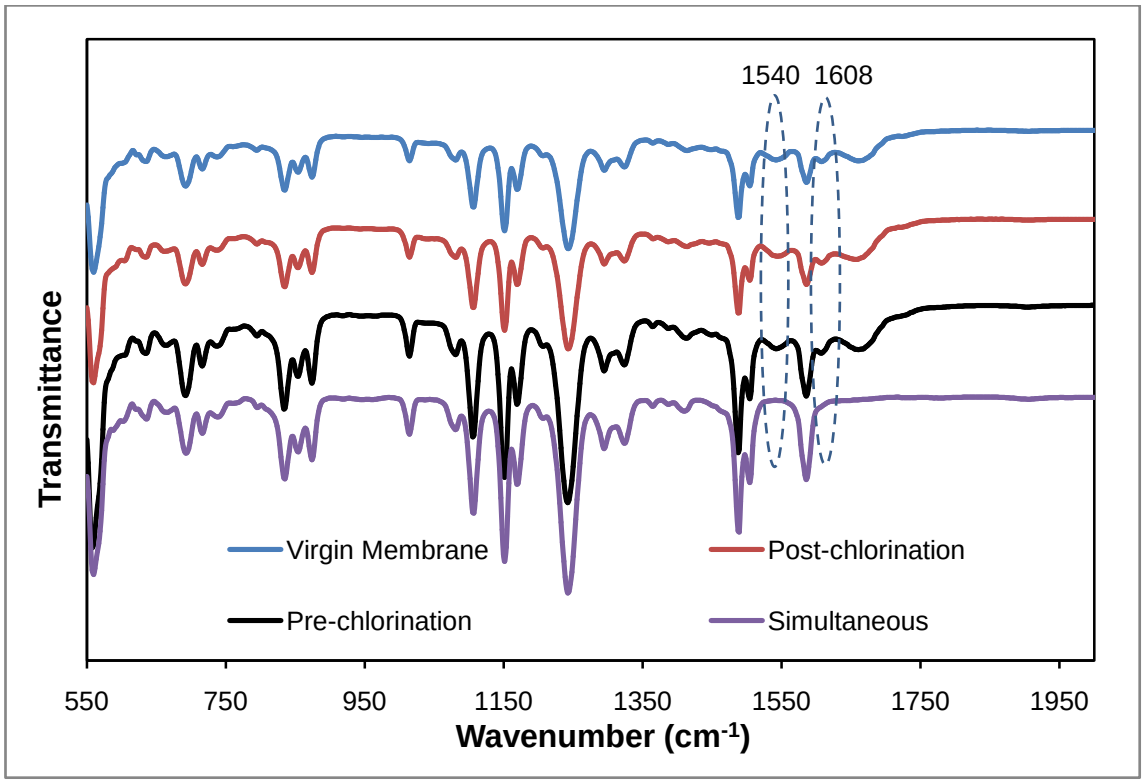


Figure 4.21: **The FTIR spectra of the membranes used in the studies.**

However, the same case did not apply to the membrane used in simultaneous. The amide bond (1540 cm^{-1}) and hydrogen bond (1608 cm^{-1}) in membrane used in simultaneous system appeared to be missing compared to the other membranes. The membrane coating layer not able to resist the attack of high concentration chlorine since the coating layer can only increases the resistance of membrane to chlorine up to a certain point, which for this membrane is around 1 ppm and as a result membrane degradation occurred.

4.5.6 Membrane Morphology

To understand more on the effect of FAC to membrane characteristic, membrane morphology study was done using field emission scanning electron microscopy (FESEM). The impact of prolonged exposure of chlorine during nanofiltration process to the membrane surface, the membrane used in both systems was analyzed by FESEM for analysis. The color of virgin membranes was white. However from visual observation, the membrane used in post-chlorination system was light brown in color resulted from what was appeared to be the residual sulphonamide derivative, while the membrane used in both pre-chlorination and simultaneous systems were dark brown. The changes in color observed for this membrane was hypothesized to be due to the chlorine attack to the membrane surface making the membrane surface structure to change.

Figure 4.22 shows the comparison of the images of membrane surfaces for all three systems. For the pre-chlorination system, only the membrane used in excess chlorine system was scanned since the residual FAC in contact with the membrane surface was higher. Contrary to what was expected, nothing significant occurred to the membrane surface used in pre-chlorination systems (Figure 4.22(a) and (d)). In fact, there was only a slight precipitation of sulphonamide observed on the membrane surface. Evidently the residual chlorine present in the membrane feed helped by partially cleaning the membrane surface from any residual sulphonamide present on the membrane surface. However, the absence of chlorine in the membrane feed in post-chlorination system resulted in the precipitation of sulphonamide on the surface (Figure 4.22(c) and (f)), thereby decreasing the flux reading over time.

However, different observation was noticed on the membrane used in simultaneous system. Like the other observation on membrane used in simultaneous system (fluxes, FTIR and salt rejection), FESEM images also confirmed that membrane degradation did in fact took place where polymer layer on the membrane surface breaks down and exposed the inner layer of the membrane.

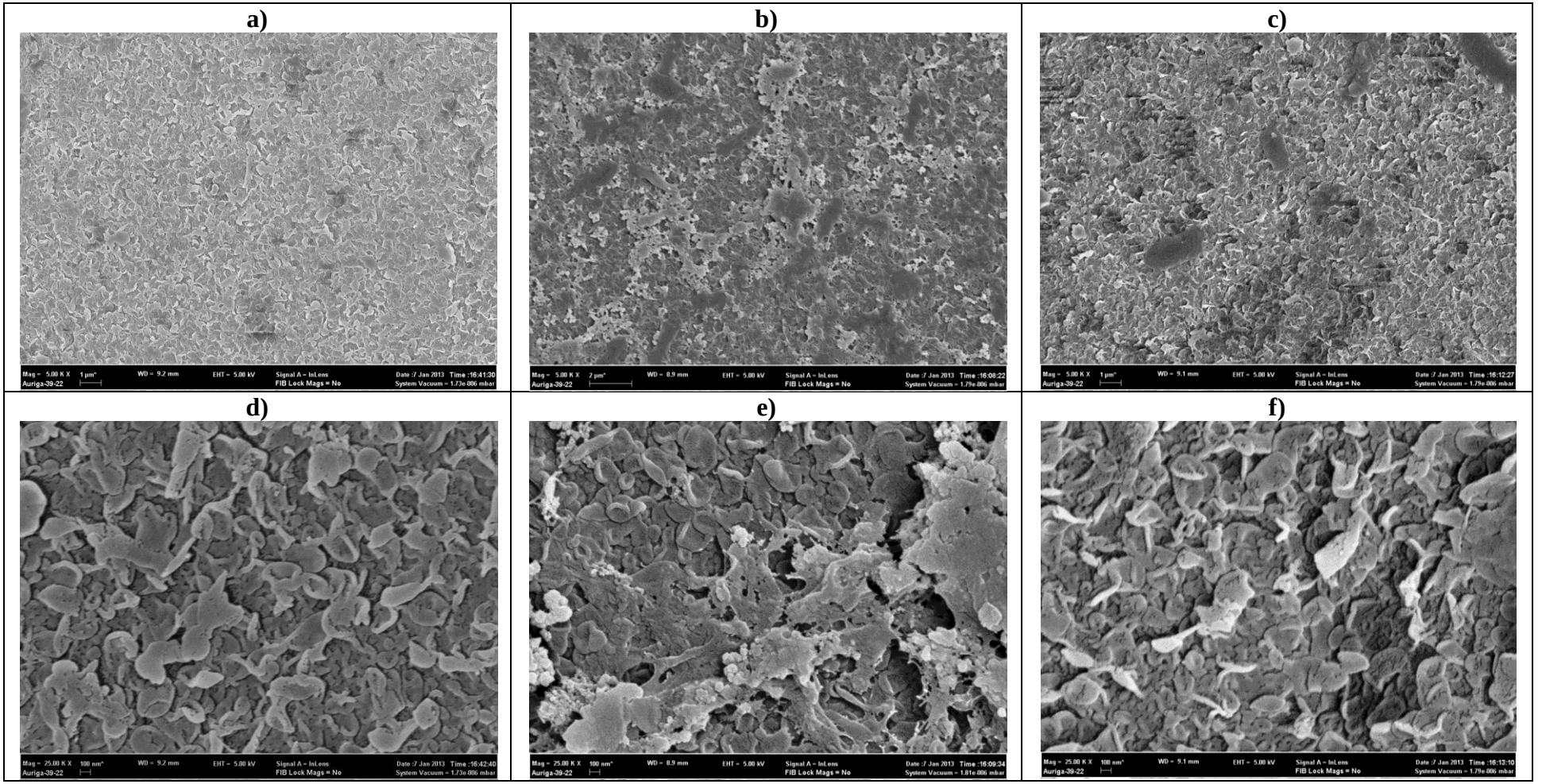


Figure 4.22: **Surface images of used nanofiltration membrane generated using field emission scanning electron microscopy: a) pre-chlorination system (5,000x), b) simultaneous system (5,000x), c) post-chlorination system (5,000x), d) pre-chlorination system (25,000x), e) simultaneous system chlorination (25,000x), and f) post-chlorination system (25,000x).**

CHAPTER 5

CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE WORK

5.1 Conclusions

The present study compares the effectiveness between pre-chlorination, hybrid and post-chlorination systems on the total removal of sulphonamide and its by-products in the combined nanofiltration and chlorination system.

The finding shows that soft quenching technique gave higher values of first order rate constant compared to normal quenching technique done elsewhere (up to factor of 3). It was also demonstrated that in the nanofiltration-chlorination system with the excess FAC, overall removal efficiency of hybrid and pre-chlorination systems were higher compared to the post-chlorination system (>99.35% & >99.87% vs. >88.31%). Nanofiltration membranes effectively removed most of the intermediate compounds and by-products formed during the reaction.

However in the case of limited FAC, removal efficiency for post-chlorination system was higher compared to other two system due to the prior nanofiltration process that effectively removed 12.5% to 79% of sulphonamide and consequently helped reduced the concentration of sulphonamide in permeate making the addition of FAC afterward an excess compared to available sulphonamide.

Majority of the reactions by-products formed during the chlorination of sulphonamide were found to have higher molecular weight compared to its original compound making these compounds efficiently removed by nanofiltration, although some of the by-products size were smaller than the molecular weight cut-off (MWCO) of nanofiltration membrane employed.

Reduced concentration of sulphonamide in pre-chlorination and hybrid systems due to chlorination process resulted in higher permeate flux compared to post-chlorination system. Residual chlorine in the membrane feed helped in increasing the membrane flux by partially cleaning the membrane. Reduced pH (pH < 5.0) in membrane feed over time due to reduction of chlorine together with the increased concentrated sulphonamide in the feed side for pre-chlorination system resulted in lower permeate flux compared to the flux for nanofiltration of chlorine only (pH 7.2), although it is still higher compared to post-chlorination system. However, the flux for nanofiltration of chlorine in ultrapure water was lower than the flux of simultaneous system. Increases of membrane flux more than the flux value of ultrapure water suggests that the membrane degradation took place from the continuous dosage of excess FAC oxidant to the surface of the membrane.

The stable salt rejection observed for membranes used in prechlorination suggests that the membranes were not significantly damaged from the chlorine exposure. Furthermore, the increases in membrane surface negativity together with the effect of pore tightening from chlorine exposure resulted in the increase of inorganic salt and sulphonamide rejection for both chlorinated membranes used in this study. It is also confirmed from the morphology study that no significant changes occurred on the membrane surface and its pore size that could significantly affects the rejection process

in pre-chlorination system. However, from the observation on salt rejection and morphology study suggested that the membrane used in simultaneous system is damaged from continuous chlorine exposure. The findings are applicable to the other compounds that have the same characteristic as sulphonamide in which the intermediate by-products that is not stable and able to retransform back to their parent compound.

5.2 Recommendations for Future Work

Currently, the concentrations of sulphonamide found in the surface water are still low and did not directly posses threat to the humankind. However, from the previous literature done, sulphonamide was found to have a higher biodegradability during water and wastewater treatment. Surprisingly in some of the water and wastewater treatment plant, concentration of sulphonamide in effluent is much higher compared to the influent. One of the chlorination reaction by-products of SMX known as NCBQ was found to have a higher toxicity compared to the parent sulphonamide. For that, toxicity study for all of the majority reaction by-products are needed to ensure that the process is not going to introduce a much more harmful chemical into the environment. Furthermore, the degradability and also the stability of the reaction by-products also need to be the main focus for the next study.

In this study, a simulated wastewater containing only sulphonamide was used as feed influent. However in an actual wastewater, there are other organic and inorganic compounds presence in the influent that could significantly react with FAC, for instance natural organic matter (NOM). NOM are known to reacts with FAC to produces disinfection by-products (DBPs) which are quite harmful to the environment. Not only

that, NOM might also compete with sulphonamide for reaction with FAC. In order to evaluate this system correctly, an actual wastewater needs to be used as feed influent.

As mentioned in the discussion on reaction rate of chlorination of sulphonamide, reaction rate for sulphonamide derivatives are not related to their molecular weight. Even though sulphonamide derivatives share the same functional group, SNM with the smallest molecular weight exhibited higher reaction rate than SMX and SDZ but slightly lower compared to SDM which have the highest molecular weight of sulphonamide derivatives studied. More analysis need to be done in order to understand what makes the reaction rate differs between sulphonamide derivatives.

Polyamide membranes are prone to degradation in the presence of FAC even at a low concentration. The polyamide membrane used in this study has a maximum FAC tolerance of 0.1ppm in continuous mode. Since this membrane is a commercial membrane that is being widely used in treatment plant, this membrane is suitable to be used as to simulate the membrane process in treatment plant. However, ceramic membrane has a higher tolerance towards FAC compared to polymer membrane. It is definitely worthwhile to use ceramic membrane for this study in the near future. Furthermore, research on chlorine resistant polymer membrane is being conducted widely and most of them showed promising results.

Currently the concentrated retentate produced from the nanofiltration process is stored in waste bottle ready to be disposed. Since sulphonamide and some of its by-products are quite toxic to the environment, disposal of the concentrated without further treatment could be harmful to the environment. Proper disposal method is needed before these wastes can be disposed.

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APPENDIX A

Standard calibration curve of sulphonamide using HPLC

In order to determine the concentration of sulphonamide, Shimadzu HPLC-UV was used for analysis. However, standard calibration curves need to be prepared first as the instrument cannot give the direct concentration values. From the analysis of ten known concentrations of each sulphonamide, graphs were plotted by taking the area under the HPLC curves against its concentrations. These produced a linear trend line known as standard calibration curve. Analysis of a standard calibration curve was repeated by using another standard samples. Average area of both reading were computed and used for the preparation of standard curve. Figure A1 shows the plotted standard calibration curves from the analysis of sulphonamide standard.

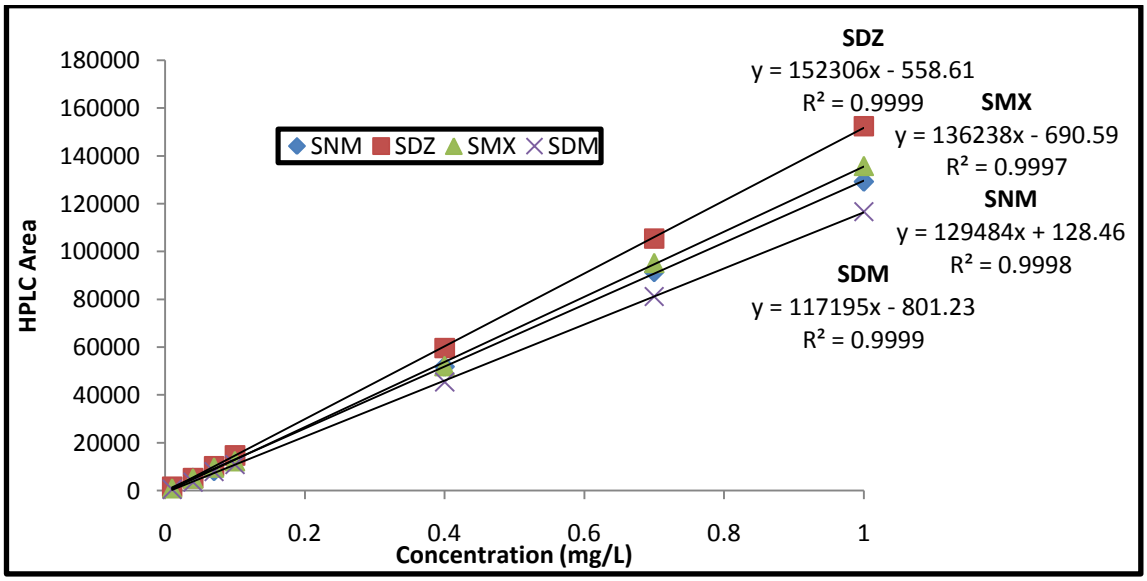

Figure A1: Standard calibration curve for studied sulphonamide

Coefficients of determination (R2) of more than 0.999 were obtained for all sulphonamide. Table A1 shows the summary for the value of the slope and its

coefficient correlation for each sulphonamide. Using the equation obtained, an exact concentration of sulphonamide (x) could be determined by substituting the area under the curve into the equation (y).

Table A1: Summary of the calibration curve equation obtained for all sulphonamide

No.	Sulphonamide	Curve Slope(m)	Coefficient Correlation (R^2)
1	Sulfanilamide	129484	0.9998
2	Sulfadiazine	152306	0.9999
3	Sulfamethoxazole	136238	0.9997
4	Sulfadimethoxine	117195	0.9999

From the entire prepared standard, sulphonamide with concentration of 700 ng/L cannot be quantified, even though it was detectable in HPLC spectra. This is due to limitation of the HPLC system in calculating a very small area under the curve. However, analysis of sulphonamide with concentration of 600 ng/L was not detected at all in HPLC spectra. This observation concluded that the Limit of Quantification (LOQ) for all studied sulphonamide is at 1 µg/L while the Limit of Detection (LOD) for sulphonamide is at 600 ng/L.

APPENDIX B

LIST OF JOURNAL ARTICLES

1. Mohd Redzuan Ramli, Nik Meriam Nik Sulaiman, Mustafa Ali Mohd & Mohamad Fairus Rabuni. (2015) Performance of chlorination process during nanofiltration of sulfonamide antibiotic. Water Science & Technology, 2015. doi:10.2166/wst.2015.367

2. Nik Sulaiman, N.M., Ramli, M.R. (2012) Comparison of the Effectiveness Between Post-Chlorination and Pre-Chlorination on Nanofiltration of Sulfonamide. Procedia Engineering, , 44, 2006-2009. doi:10.1016/j.proeng.2012.09.024

3. Mohd Redzuan Ramli, Nik Meriam Nik Sulaiman. Effect of residual chlorine on the rejection of sulfonamide antibiotics and its by-products using nanofiltration. Desalination and Water Treatment. Under review

LIST OF CONFERENCE PROCEEDINGS

1. Ramli, M.R. and Nik Sulaiman, N.M. 2012. Effect of Pre-oxidation on Removal of Sulfonamide Antibiotics from Simulated Wastewater by Nanofiltration Membrane, Proceeding of Green Process Engineering (GPE) 2011, 6 – 8 December 2011, Kuala Lumpur, Malaysia.

2. Ramli, M.R. and Nik Sulaiman, N.M. 2012. Comparison on the Effectiveness between Post - Chlorination System and Pre-Chlorination System on Nano Filtration of Sulfonamide. Proceeding of Euro Membrane 2012 Conference, 23 - 27 September 2012, London, United Kingdom.