OCCURRENCE OF ANTIBIOTIC AND TREATMENT PERFORMANCE OF DECENTRALIZED AND CONVENTIONAL SEWAGE TREATMENT PLANTS

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DEDICATION

This thesis is dedicated to my parents, family members, fiancée, supervisors and friends without whom none of my success would be possible.

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ABSTRACT

Antibiotics are widely used in human society and have been frequently detected in sewage treatment plants (STP). However, the fate of antibiotics in these STPs is limited, particularly in Southeast Asian countries. Therefore, this study was conducted to evaluate the removal performances of six selected STPs on selected wastewater quality parameters and four frequently prescribed antibiotics (ampicillin, ciprofloxacin, erythromycin and sulfamethoxazole). The mass flow, mass balance and removal pathways analysis of the antibiotics in these STPs were conducted in detail. The insight into the relationship between the removals of wastewater quality parameters and antibiotics was provided. Sewage samples were taken at each stage of six STPs, comprising of two decentralised treatment plants (Imhoff tanks (IT)), four conventional treatment plants (three extended aerations (EA) and one conventional activated sludge (CAS)) in Johor Bahru district. Liquid and sludge samples were pre-treated using solid phase extraction and ultrasonicate extraction, respectively, followed by their quantification using UHPLC-MS according to USEPA Method 1694. Quality control experiment was done for the selected antibiotics with internal surrogate standards. The findings showed that most of the conventional wastewater constituents were better removed in conventional treatment systems compared to decentralised treatment system. The findings revealed that ampicillin, ciprofloxacin, erythromycin and sulfamethoxazole were detected in most wastewater samples, including influent, secondary effluent, final effluent and sewage sludge samples. The antibiotic concentrations in the wastewater and sludge ranged from 4.2 ng/l to 2,690 ng/l and 1.7 ng/g to 317.4 ng/g, respectively. Between -26.4% to 99.9% of the antibiotics were removed in all STPs, depending on the process employed. A detailed antibiotic mass flow was conducted in EA and IT plants. An estimate of 45.6 g of ampicillin, 76.7 g of ciprofloxacin, 60.0 g of erythromycin and 225.4 g of sulfamethoxazole were discharged into the receiving river annually. The mass balance analysis indicated that biodegradation is the major route for the removal of all antibiotics studied. Sorption is only responsible for minor removal of ciprofloxacin, erythromycin and sulfamethoxazole. Statistical analysis showed that AMP and ERY removals were highly related with organic and solid removals while the removal of CIP and SMX were highly related with nutrient removal only. However, these relationships were insignificant due to small number of samples. As a conclusion, this study provided a preliminary evaluation on the removal of antibiotics in each stage of conventional and decentralised STPs. This work showed that conventional treatment system has better removal performance on wastewater quality parameters compared to decentralised treatment system. However, the removal of antibiotics accomplished by both conventional treatment systems is not significantly superior than that of decentralised treatment systems. Both systems are insufficient to prevent the discharge of antibiotics into the environment.

ABSTRAK

Antibiotik digunakan secara meluas dalam masyarakat dan ia telah dikesan di loji rawatan kumbahan (STP). Walau bagaimanapun, pengetahuan tentang nasib antibiotik dalam STP adalah terhad, terutamanya di negara-negara Asia Tenggara. Kajian ini dijalankan bagi menilai prestasi penyingkiran beberapa parameter kualiti air kumbahan dan empat antibiotik yang lazim digunakan (ampisillin (AMP), siprofloksasin (CIP), eritromisin (ERY) dan sulfametoksazol (SMX)) di enam buah STP terpilih. Analisa aliran jisim, keseimbangan jisim, dan jalan penyingkiran antibiotik di STP telah dijalankan secara terperinci. Hubung kait di antara penyingkiran parameter air kumbahan dan antibiotik diberikan. Sampel air kumbahan telah diambil di setiap bahagian proses rawatan di dua buah STP tidak berpusat (tangki Imhoff (IT)) dan empat buah STP konvensional (tiga sistem pengudaraan lanjutan (EA) dan satu sistem konvensional enapcemar teraktif (CAS)) di daerah Johor Bahru. Pra-rawatan telah dilakukan bagi semua sampel air dan enapcemar dengan menggunakan pengekstrakan fasa pepejal dan pengekstrakan ultrasonik sebelum penentuan kuantiti dibuat dengan menggunakan kromatografi cecair berprestasi tinggi- spectrometer mass (UHPLC-MS) berdasarkan Kaedah 1694 USEPA. Ujian kawalan kualiti telah dijalankan bagi antibiotik terpilih dengan mengikut piawaian pengganti dalaman. Hasil kajian menunjukkan bahawa STP konvensional mempunyai prestasi penyingkiran parameter kualiti air kumbahan yang lebih baik berbanding dengan STP tidak berpusat. Selain itu, antibiotik AMP, CIP, ERY dan SMX telah kesan di dalam semua sampel air sisa termasuklah sampel influen, efluen dan sampel enapcemar. Antibiotik berkepekatan di antara 4.2 ng/l dan 2,690 ng/l dikesan dalam air sisa manakala antibiotik berkepekatan di antara 1.7 ng/g to 317.4 ng/g telah dikesan dalam enapcemar. Penyingkiran antibiotik di antara -26.4% dan 99% didapati di semua STP, bergantung kepada proses yang digunakan. Analisa aliran jisim antibiotik telah dilaksanakan secara terperinci untuk sistem EA dan IT. Dianggarkan sebanyak 45.6 g AMP, 76.7 g CIP, 60.0 g ERY dan 225.4 g SMX, telah dilepaskan ke dalam sungai setiap tahun. Analisis keseimbangan jisim antibiotik menunjukkan penguraian bio adalah cara penyingkiran antibiotik yang utama. Penjerapan hanya bertanggung jawab menyingkirkan sedikit CIP, ERY dan SMX. Analisis statistik menunjukkan bahawa wujudnya hubungan yang kuat antara penyingkiran AMP dan ERY dengan penyingkiran organik dan nutrien. Selain itu, penyingkiran CIP dan SMX juga mempunyai hubungan dengan penyingkiran nutrien. Walau bagaimanapun, hubungan tersebut adalah tidak ketara disebabkan bilangan sampel yang kecil. Kesimpulannya, kajian ini menunjukkan bahawa STP konvensional mempunyai prestasi penyingkiran parameter kualiti air kumbahan yang lebih baik berbanding dengan STP tidak berpusat. Tetapi, tidak ada bukti yang menunjukkan prestasi penyingkiran antibiotik di STP konvensional adalah lebih baik daripada STP desentralisasi. Kedua-dua sistem STP tidak manpu untuk menghalang pelepasan antibiotik ke persekitaran.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AMP	-	Ampicillin
ANOVA	-	Analysis of variance
ARB	-	Antibiotic resistance bacteria
ARG	-	Antibiotic resistance gene
BOD	-	5 days- biochemical oxygen demand
CAS	-	Conventional activated sludge
CIP	-	Ciprofloxacin
CO2	-	Carbon dioxide
DDD	-	Defined daily dose
DNA	-	Deoxyribonucleic acid
EA	-	Extended aeration
EC	-	European Communities
ERY	-	Erythromycin
HRT	-	Hydraulic retention time
IPASA	-	Centre for Environmental Sustainability and Water Security
IT	-	Imhoff Tank
K_d	-	Solid-water distribution coefficient
KW	-	Kruskal-Wallis test
LC-MS/MS	-	Liquid chromatography tandem mass spectrometry
$LogP_{ow}$	-	logarithm octanol/water partition coefficient
MLSS	-	Mixed liquor suspended solid
MOH	-	Ministry of Health Malaysia
MQL	-	Method quantification limit
MW	-	Mann-Whitney test
NA	-	Not available

ND	-	Not detected
PBP	-	Ribosomal penicillin binding proteins
pKa	-	Dissociation constant
PPCP	-	Pharmaceutical and personal care products
RNA	-	Ribonucleic acid
RSD	-	Relative standard deviation
SCOD	-	Soluble chemical oxygen demand
SEA	-	Southeast Asia
SMX	-	Sulfamethoxazole
Sp	-	Spearman correlation test
SRT	-	Solid retention time
STP	-	Sewage treatment plant
TCOD	-	Total chemical oxygen demand
Temp	-	Temperature
TN	-	Total nitrogen
TNT	-	Test and Tube
TP	-	Total phosphorus
TSS	-	Total suspended solid
TVS	-	Total volatile solid
UHP-LC/MS	-	Ultrahigh performance liquid chromatography tandem mass spectrometry
UTM	-	Universiti Teknologi Malaysia
WHO	-	World Health Organization

LIST OF SYMBOLS

Q	-	Flow rate
r^2	-	linearity
$T_{1/2}$	-	Half-life
n	-	Freundlich coefficient
K_1	-	Reaction rate
K_{biol}	-	Biotransformation coefficient

LIST OF APPENDICES

CHAPTER 1

INTRODUCTION

1.1 Preamble

The effectiveness of antibiotics against bacterial infection have rendered exponential increase in consumption of antibiotics around the globe. During the past 15 years, the global consumption of antibiotics has increased from 21.1 billion to 34.8 billion defined daily dose (DDD) (Gelband et al., 2015). After the consumption of antibiotic, a portion of the consumed antibiotic will be excreted from human body and discharged into sewerage system. This consequently led to the frequently found of various types of antibiotics in the influent of sewage treatment plant (STP), ranging from ng/L to μg/L level (Le et al., 2018; Tran et al., 2016; Radjenović et al., 2009; Gulkowska et al., 2008; Brown et al., 2006; Göbel et al., 2005).

Despite conventional treatment system being currently adopted as main treatment technology, decentralised treatment system is employed in urban and rural areas of many countries (Nguyen et al., 2018; Capodaglio, 2017; Yacob et al., 2017; Istenic et al., 2015). For example, decentralised treatment system accounted for 50% of the total STP and serving 1.0 million populations in Malaysia (IWK, 2020). Meanwhile, developed countries such as United States, have decentralised treatment system serving approximately 60 million people (Nelson, 2005).

Unfortunately, most of the conventional STPs are incapable to achieve complete removal of antibiotics and only a portion of these antibiotics will be removed during the treatment process (Le et al., 2018; Alvarino et al., 2014). The untreated antibiotics will eventually be discharged into receiving water body. As a consequence, aquatic organisms and human are exposed to high risk due to the presence of the antibiotic's residue (Hu et al., 2018; Papageorgiou et al., 2016; Kosma et al., 2014).

The toxicity of antibiotic residue varies depending on the types of antibiotic exposure. Many acute and chronic adverse effects were reported such as transfer of antibiotic resistant bacteria to the human, autoimmunity, carcinogenicity (sulfamethazine and oxytetracycline), mutagenicity, nephropathy (Gentamicin), hepatotoxicity, reproductive disorders, bone marrow toxicity (Chloramphenicol) and allergy (Penicillin) (Priyanka et al., 2017; Pomati et al., 2006). More importantly, the development of antibiotic resistance bacteria (ARB) and antibiotic resistance gene (ARG) could be easily triggered by antibiotic residue at environmental relevant concentration as reported in many previous studies (Hanna et al., 2018; Le et al., 2018; Calero-Cáceres et al., 2017; Keen et al., 2017; Qiao et al., 2017). Worldwide, the development and spread of antibiotic resistant bacteria/resistance genes has become a serious and growing threat to modern medicine and is considered as one of the leading health concerns of the 21st century (WHO, 2019).

In this context, many countries have initiated monitoring program on the antibiotic removal capability of STPs. Recently, few types of antibiotics have been listed as hazardous substances in the *list of priority substances in the field of water policy* by the European Communities (EC) (EC, 2018; EC, 2015). In Malaysia, the discharge of sewage is regulated by the Environmental Quality (Sewage) Regulations 2009, Environmental Quality Act 1974 and the operators of the STP are responsible in ensuring that the effluent from the STP complies with the legislative requirement (DOE, 1974). However, currently, none of the regulation is in force to regulate the limit for antibiotics discharge into the environment.

In general, STP comprised of several treatment stages, which include primary, secondary and tertiary treatments. During the treatment in STP, different portion of antibiotic is removed in each of the treatment stage and it is mostly removed through biotic (biodegradation) and abiotic (sorption) pathways. Due to the differences in the design and operation of each treatment stage, the removal efficiency of the antibiotics contributed by each stage varies accordingly (Östman et al., 2018; Batt et al., 2007). In Malaysia, most of the STPs consist of two stages without tertiary treatment. The removal of antibiotics thus fully depends on the currently existing processes. This raises the need and concern on the investigation of removal efficiency of the antibiotics by each treatment stage of the STPs.

1.2 Problem Statement

Many previous researches have been conducted on the effectiveness of STP in antibiotic removal. However, these studies only focused on conventional STP such as activated sludge system and membrane bioreactor. Decentralised treatment system such as septic tank and it modified system (i.e. imhoff tank) apparently missing in previous study. This information is important as these decentralised treatment systems are still commonly employed in rural area and small community of many countries as main treatment system. Hence, to have a clearer idea on how these systems remove antibiotic in wastewater is essential to prevent continue discharge of antibiotic to environment.

The type and concentration of antibiotics detected in the influent of STPs varies considerably between region and country. Despite extensive researches being carried out on the occurrence of antibiotics in the influent of STPs, the types and concentration of antibiotics detected in STP influent varied between the studies regardless of treatment systems employed. The significant variation of antibiotic types and concentrations in STPs' influent between regions could be due to factors such as antibiotics consumption pattern, seasonal and hourly fluctuation and the effect of STP scale. The variation between regions renders the investigation results from other studies not suitable to be fitted in Malaysia scenario. Hence, this study is important as to provide a better understanding on the presence of antibiotics in the influent of STP in Malaysia.

Many countries such as United Stated, China, Spain, Finland, Japan and Singapore had initiated the investigation on the antibiotic removal capability of STPs in their respective countries. This information is important as it will provide a better understanding on the actions that need to be taken to minimize the antibiotic discharge into environment. Apparently, as the investigation on the antibiotic removal capability of STP in tropical climate countries have only been carried out in Singapore, further study in this area is therefore crucial.

In Malaysia, different types of treatment system have been employed in STP consisting of old and new technologies. Each system comprised of different processes with different capabilities. There is a need to understand how these processes and systems respond to different types of antibiotics and the type of removal mechanisms and pathways that are involved in the removal process with regards to the tropical climate. Furthermore, as antibiotics are expensive to analyse, it is important to explore the relationship between the removal of the commonly monitored wastewater quality parameters and the antibiotics.

1.3 Objectives

The aim of this study is to investigate the occurrence and behaviour of selected antibiotics in targeted STPs. The study objectives are:

i. To evaluate the occurrence concentration of targeted antibiotics (Ampicillin (AMP), ciprofloxacin (CIP), erythromycin (ERY) and sulfamethoxazole (SMX)) in the targeted STPs and the effectiveness of selected conventional and decentralized sewage treatment processes on the removal of selected antibiotics.

ii. To determine the behaviour and removal pathway of the targeted antibiotics in STP through mass balance analysis.

iii. To relate the performance of the conventional treatment process in removing wastewater quality parameters and the selected antibiotics.

1.4 Scope of study

The study was conducted at six selected STPs in Johor Bahru district throughout a research period of eight months (December 2018 – August 2019). The selected types of STP include extended aeration (EA), imhoff tank (IT) and conventional activated sludge (CAS) which are commonly used in Malaysia.

This study focused on four types of antibiotic namely AMP, CIP, ERY and SMX being the most common used antibiotics around the globe (World Health Organization, 2018). Additionally, other wastewater quality parameters including chemical oxygen demand (COD - total and soluble), biochemical oxygen demand (5d-BOD), total suspended solid (TSS), total volatile solid (TVS), ammonia-N, nitrite-N, nitrate-N, total nitrogen (TN) and total phosphorus (TP) were also monitored. They were monitored at the influent, intermediate treatment stages and effluent of the treatment plants. The antibiotics within the solid/biomass were also quantified to determine the sorption capacity of the antibiotics onto these solids. The separation and quantification of the antibiotics were carried out at Monash University LC-MS/MS Laboratory, while the samples preservation, wastewater quality parameters analysis and samples pre-treatment (solid phase extraction and ultrasonicate extraction) were conducted at IPASA Environmental Engineering Laboratory, UTM.

The removal efficiencies of wastewater quality parameters and antibiotics of the targeted STPs were compared and correlated. The mass balance analysis of antibiotics throughout the process of STPs were conducted to understand the fate and removal pathways of the antibiotics.

1.5 Significance of study

Extensive research has showed the ineffective treatment of antibiotics by STP in many country and region (Verlicchi et al., 2012; Li and Zhang, 2011). While many studies have been conducted elsewhere, such study is apparently lacking in Southeast

Asia region (SEA), such as Malaysia. Therefore, the significances of this study are listed as follows:

1. The findings of this study would provide a better understanding on the removal capability of antibiotics by conventional and decentralised treatment systems. Furthermore, as decentralised treatment systems serve as a vital part of the sewerage system in Malaysia and many countries, the outcome of this work would be significantly beneficial.

2. The findings from mass balance analysis would allow us to understand the contribution of each treatment stage at the STP in removing the antibiotics. This would also enhance our understanding on the removal pathway of the antibiotics within the treatment process.

3. Investigation on the removal efficiency of the STPs with regards to the conventional wastewater quality parameters would provide a better understanding on the efficiency of different treatment systems in abiding to the regulations set by the authorities. Furthermore, the examination of the relationship between wastewater quality parameters removal and antibiotics removal would allow us to understand the simultaneous process that occurs during the removal process. The relationship would also provide a cheaper approach in determining the removal of antibiotics from the wastewater.

1.6 Limitation and assumption

There are few limitations and assumptions used in this work and they are as follows:

(1) The studied STPs in this work are located in Johor District only. Therefore, the findings from this work might not represent the situation of whole Malaysia.

(2) Grab sampling method was used in this work instead of composite sampling. This is based on the assumption that all STPs are operating under steady state.

1.7 Organization of thesis

This thesis consists of five chapters. The gap on the antibiotic removal in decentralised treatment plant and the importance on filling these gaps are discussed in the first chapter. The second chapter focuses on the literature review, mainly discusses on the occurrence of antibiotics in surface water and wastewater, the removal mechanisms of antibiotics, the overall antibiotics removal in treatment plants and the factors affecting the antibiotics removal during treatment process. The third chapter explains the methodology used for this study and the detailed procedure of antibiotics recoveries, detections and quantifications. Chapter Four discusses the findings of the study, according to each objective. Finally, Chapter Five shows the conclusions and recommendations for future research.

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