International Biodeterioration & Biodegradation 102 (2015) 398–401

Contents lists available at ScienceDirect

International Biodeterioration & Biodegradation

journal homepage: www.elsevier.com/locate/ibiod

# A case study of antibiotic wastewater treatment by using a membrane biological reactor system

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ARTICLE INFO

*Article history:*
Received 28 December 2014
Received in revised form
10 April 2015
Accepted 10 April 2015
Available online 6 May 2015

*Keywords:*
Antibiotic wastewater
Imipenem
Cilastatin
MBR

ABSTRACT

The antibiotic medicines were widely applied for therapy use or prevention of flu infection. The residual antibiotic medicine might be present in wastewater and sludge during the manufacturing processes, and it is liable to intentionally release to the surroundings to harm to the environment or threaten human health. This study selected a carbapenem antibiotic manufacturing plant as case study to investigate the feasibility of antibiotic wastewater treatment by an MBR system. The characteristics of imipenem antibiotic wastewater showed the average concentrations of 3929 mg $L^{-1}$ COD and 2383 mg $L^{-1}$ BOD. The characteristics of cilastatin antibiotic wastewater showed the average concentrations of 4245 mg $L^{-1}$ COD and 1760 mg $L^{-1}$ BOD. The combined antibiotic wastewater was treated by an MBR system, and the treatment efficiencies are 92.5% for BOD removal, 96.0% for COD removal and 81.5% for suspended solid removal. The inflow wastewater of the MBR system contains 4.97 ng $L^{-1}$ imipenem and 3.77 ng $L^{-1}$ cilastatin, and the outflow concentrations through MBR treatment are ND for imipenem and 0.02 ng $L^{-1}$ for cilastatin. The treatment efficiencies of antibiotic wastewater are more than 99.9% through MBR treatment.



## Introduction

Antibiotics have been frequently used in the treatment and prevention of infectious disease, as well as to treat humans and animals (Tambosi et al., 2010; Dorival-Garcia et al., 2013; Li et al., 2013). Recent studies showed that trace amounts of antibiotics have been detected in various types of aqueous environments, such as water, reservoirs, lakes, fish hatcheries and the respective sediments, and in ground water (Lin and Tsai, 2009; Lin et al., 2010a; Lin et al., 2011; Wang and Lin, 2012, 2014; Lee et al., 2014). The spread of antibiotics can cause bacteria in the environment to develop resistance to drugs, resulting in ineffective treatments involving the first and the second-line antibiotics. Continual treatments with the last-line potent antibiotics can greatly increase bacterial resistance to the drugs in the environment, and ultimately result in the ineffectiveness of medication treatments (Munir et al., 2011; Gao et al., 2012; Qiu et al., 2013). Therefore, the fate of antibiotics in the environment, categorized as a type of pharmaceutical and personal care product pollutant, has gained considerable attention recent years (Lin et al., 2010b, 2011; Li et al., 2013).

A membrane bioreactor (MBR) is a wastewater treatment device that integrates activated sludge and membrane technology. By utilizing the ability of membranes to separate solid and liquid wastes, MBRs possess the equivalent function of settling tanks and sand filters in activated sludge processes, which can solve the problem of ineffective treatment caused by inadequate sedimentation of sludge. Through improving the stability of biological treatments, MBRs are suitable for the treatment of wastewaters containing non-biodegradable pollutants, highly concentrated pollutants, and pollutants exhibiting large loading variation. Accordingly, MBRs are gradually gaining attention because of their advantages, such as small land occupation, fast processing speed, limited sludge production, and high-quality effluents (Tambosi et al., 2010; Sahar et al., 2011; Dolar et al., 2012; Dorival-Garcia et al., 2013; Qiu et al., 2013).

The manufacturing process of antibiotics is complex, including sequential steps of synthesis, filtration, refinement, extraction, crystallization, centrifuge, drying, and packaging. Antibiotic wastewater contains a high concentration of organic solvents and large amounts of solid suspensions that can cause high turbidity

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http://dx.doi.org/10.1016/j.ibiod.2015.04.018
0964-8305/

and multifarious composition. Furthermore, antibiotic residuals in wastewater may suppress the activity of the microbes presented in biological treatments, increasing the difficulty of treatments. Therefore, the objective of this study was to monitor chemical oxygen demand (COD), biological oxygen demand ($BOD_5$), suspended solids (SS), and antibiotic concentrations of wastewater released from an antibiotic manufacturing factory. This study also examined the feasibility of employing an MBR system to treat antibiotic-containing wastewater.

## Methods and materials

### *Wastewater treatment from a pharmaceutical factory*

This study selected an antibiotic manufacturing factory located at Southern Taiwan Science Park (Tainan, Taiwan) as study case. This factory primarily produces Tienam, which contains carbapenems. Tienam is the last-line antibiotic containing a mixture of imipenem and cilastatin at a 1:1 ratio w/w. Imipenem ($C_{12}H_{17}N_3O_4S \cdot H_2O$) is a broad-spectrum antibiotic that acts as a competent inhibitor for cell wall synthesis, and is effective against most gram-positive and gram-negative aerobic and anaerobic bacteria. Cilastatin ($C_{16}H_{25}N_2NaO_5S$) is a specialized enzyme inhibitor that can suppress the metabolism of imipenem in the liver, increasing the concentration of imipenem in the urinary tract.

Tienam manufacturing utilizes batch production, with each batch requiring five to seven days of production time. The wastewater stream discharged from imipenem manufacturing (hereafter referred to as imipenem wastewater) first passed through a 0.45-μm membrane filter (MF), and then merged with another wastewater stream discharged from cilastatin manufacturing (hereafter referred to as cilastatin wastewater). The ratio of wastewater discharged from imipenem and cilastatin manufacturing was approximately 3:2. Fig. 1 outlined the overall wastewater treatment processes through the MBR system. The volume of wastewater passing through the treatment system was 500 CMD. The pH value of the wastewater was maintained between 6.5 and 8. Wastewater flew through an aeration tank, aerobic bioreactor, primary settling tank, and MBR equalization surge tank, and ultimately into the MBR reaction tank. Treated effluent then flew through a discharge tank. The MBR system utilized a POREFLON membrane, which is an immersive type of PTFE microfiltration membrane module with 0.2-μm pores, and manufactured by Sumitomo Electric Fine Polymer Inc. The effective volume of the reaction tank was 217 $m^3$, and the retention time was 10.4 h.

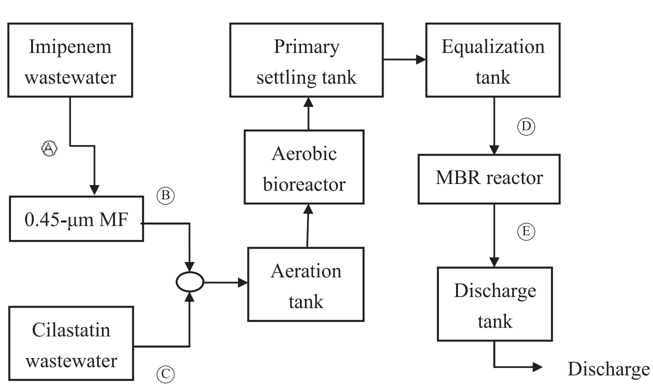


**Fig. 1.** Schematic diagram of antibiotic wastewater treatment system and sampling site.

### *Water quality monitoring*

Fig. 1 illustrates the sampling sites for water quality monitoring. Sampling Site A was located at the discharge point of imipenem wastewater, and Sampling Site B was located at the point where the imipenem wastewater is filtered through the 0.45-μm filter. Sampling Site C was located at the discharge point of cilastatin wastewater. Sampling Sites D and E were located in front of and behind the MBR reaction tank, respectively. SS, $BOD_5$, COD, and the concentrations of imipenem and cilastatin were analyzed to monitor water quality. Sample collection and analysis were performed once per week, for a total of 10 weeks.

The quantification of SS, $BOD_5$ and COD in water samples followed the procedures of Taiwan EPA NIEA-W210.58A, NIEA-W510.55B and NIEA-W517.52B standard analysis methods, accordingly (Taiwan EPA, 2009, 2011, 2013). The COD analysis utilized a spectrophotometer coupled with COD digestion vials manufactured by Hach Company. Duplicated sample analysis for COD is performed once per 10 samples and the RSD is within 20%. Referring to Taiwan EPA NIEA-W543.50B and NIEA-D902.09 standard analysis methods, the selected antibiotic manufacturing factory developed the analysis method for imipenem and cilastatin quantification by Liquid chromatography, which is equipped with an ultraviolet detector and utilizes acetonitrile as the eluent (Taiwan EPA, 2012, 2014). Regarding the chromatography of imipenem, a LiChrosorb RP-18 column (250*4.6 mm, 5 μm) was used and the wavelength was set at 254 nm, whereas an ODS-3V Inertsit column (250*4.6 mm, 5 μm) and a wavelength of 210 nm were used for the chromatography of cilastatin. Standard check analysis for antibiotics is performed every day and the RSD is within 10%.

## Results and discussions

### *Characteristics of wastewater released by Tienam antibiotic manufacturing*

Tienam is composed of imipenem and cilastatin at a mixture ratio of 1:1 (w/w). The pH value of imipenem wastewater was between 6.8 and 7.3. Fig. 2 showed SS, $BOD_5$, and COD of Sampling Sites A and B. Regarding imipenem wastewater, SS was between 16 and 32 mg $L^{-1}$ with an average value of 23.7 mg $L^{-1}$; COD was between 2682 and 5428 mg $L^{-1}$ with an average concentration of 3929 mg $L^{-1}$ and a standard deviation of 866 mg $L^{-1}$. $BOD_5$ was between 1282 and 3482 mg $L^{-1}$ with an average concentration of 2383 mg $L^{-1}$ and a standard deviation of 776 mg $L^{-1}$; the average $BOD_5$/COD value was 0.6. For the 0.45-μm filtered imipenem wastewater, the removal efficiency of SS, $BOD_5$, and COD was 17.3%, 5.4%, and 3.8%, respectively; indicating that the 0.45-μm MF was ineffective in removing pollutants. The pH value of cilastatin wastewater was between 6.8 and 7.3. Fig. 3 presented the SS, $BOD_5$, and COD of Sampling Site C. Regarding cilastatin wastewater, SS was between 4 and 21 mg $L^{-1}$; COD was between 2262 and 4607 mg $L^{-1}$ with an average concentration of 4245 mg $L^{-1}$ and a standard deviation of 1484 mg $L^{-1}$. $BOD_5$ was between 617 and 3246 mg $L^{-1}$ with an average concentration of 1760 mg $L^{-1}$ and a standard deviation of 750 mg $L^{-1}$; the average $BOD_5$/COD value was 0.41.

According to the characteristics of imipenem and cilastatin wastewater, the wastewater discharged from antibiotic manufacturing contained high concentration of COD, but exhibited a low $BOD_5$ to COD ratio, indicating that the organic wastewater discharged from this factory was not biodegradable.

Fig. 4 showed the concentration of imipenem and cilastatin in wastewater discharged from this factory. The concentration of