Chemical Engineering Journal 339 (2018) 153–161

Contents lists available at ScienceDirect

Chemical Engineering Journal

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

Removal of cytostatic drugs from wastewater by an anaerobic osmotic membrane bioreactor

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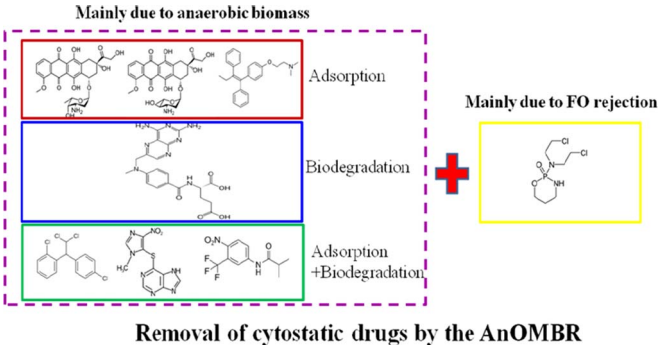
HIGHLIGHTS

- AnOMBR achieved excellent cytostatic drugs removal for FO membrane and sludge.
- Dox, Epi and Tam were nearly completely removed by adsorbing to anaerobic sludge.
- Met and CP were mainly removed by biodegradation and FO rejection, respectively.
- Mit, Aza and Flu were removed by both biodegradation and adsorption.
- Cytostatic drugs had an inhibition to the microbial activity in the AnOMBR.

GRAPHICAL ABSTRACT



Removal of cytostatic drugs by the AnOMBR

ARTICLE INFO

Keywords:
Cytostatic drugs
Osmotic membrane bioreactor
Forward osmosis
Anaerobic bioreactor
Wastewater treatment

ABSTRACT

Cytostatic drugs, mainly used as chemotherapy compounds, can pose serious threats to aqueous ecosystem and human health once released into the natural environment. We investigated the use of an anaerobic osmotic membrane bioreactor (AnOMBR) for removing cytostatic drugs from wastewater. The AnOMBR utilizes a dense forward osmosis (FO) membrane in an anaerobic digester with prolonged sludge retention time (60 days). The high rejection of the FO membrane combined with the extended organic retention time in the reactor ensured high removal rates (more than 95.6%) for all the eight cytostatic drugs investigated. With regard to their removal routes in the AnOMBR, the eight cytostatic drugs can be divided into several groups. Doxorubicin, Epirubicin and Tamoxifen were nearly completely removed through the adsorption of anaerobic sludge, while Methotrexate and Cyclophosphamide were mainly removed by biodegradation and FO rejection, respectively. In addition, Mitotane, Azathioprine and Flutamide were removed by both biodegradation and adsorption. This work provides critical insights into the removal mechanisms of high-retention AnOMBRs.

1. Introduction

Trace organic compounds (TOrCs) including personal care products, endocrine-disrupting chemicals, pharmaceutically active compounds, disinfection byproducts and industrial chemicals have gained increasing concerns for their significant threats to the environment and human health [1,2]. Among the different types of TOrCs, cytostatic drugs (also known as antineoplastic drugs) are a broad group of chemotherapy compounds mainly applied for tumor treatments [3,4]. These drugs and their human metabolites can directly enter into the

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https://doi.org/10.1016/j.cej.2018.01.125
Received 27 November 2017; Received in revised form 19 January 2018; Accepted 21 January 2018

water cycle from the hospital effluent, household wastewater, production discharge and drug waste disposal [3–7]. As a final barrier, wastewater treatment plant plays a critical role in preventing their discharge to the environment [3].

Previous studies have demonstrated that the conventional wastewater treatment technologies such as activated sludge process are not able to achieve a satisfactory removal of cytostatic drugs on the basis of biodegradation and adsorption to biomass [3,8]. Membrane bioreactors (MBRs) have been applied as an alternative technology for removing cytostatic drugs [9–12]. Their removal efficiency varied among different cytostatic compounds, and those more hydrophilic and less biodegradable compounds are likely to appear in the treated effluent. For example, up to 90% of hydrophobic anthracyclines were removed primarily due to adsorption to sewage sludge [11], while only moderate elimination was achieved in the same system for the more hydrophilic cisplatin and carboplatin (51% and 63%, respectively) [9]. Kovalova et al. [12] observed a low elimination efficiency (< 20%) for cyclophosphamide through a MBR system fed with hospital's sanitary wastewater. In order to address the low removal of more hydrophilic and less biodegradable cytostatic drugs, dense reverse osmosis (RO) membrane or tight nanofiltration (NF) membrane has been applied [3]. Previous studies have reported that thin film composite NF and RO membranes can efficiently reject most of the negatively-charged pharmaceuticals, while the rejection of neutral compounds mainly depends on their molecular weights [13–16]. However, related studies for cytostatic drugs are very limited [3], which indicates the need for further research efforts.

Recent achievements in the membrane technology have demonstrated forward osmosis (FO) as an effective alternative to conventional membrane processes for seawater desalination and water reclamation [17–19]. A typical FO membrane has a dense active layer with rejection properties on pair with RO membranes and is able to retain organic matter including small molecular compounds as well as nitrogen and phosphorus [17–22]. A recent review reports the FO removal of some 70 TOrCs [1]. Nevertheless, TOrCs are merely physically concentrated (as in the case of RO and NF) rather than chemically or biologically degraded.

We are inspired by the latest development of osmotic membrane bioreactors (OMBRs), where a dense FO membrane is used to retain dissolved organic matter in addition to suspended solids and biomass [23–34]. Due to the high retention nature of FO membrane, the residence time of TOrCs can theoretically approach the sludge retention time (SRT) in an OMBR, instead of the hydraulic retention time (HRT) as in a conventional MBR. This extended TrOC exposure time, i.e., trace organic retention time (TrORT), to the biological treatment may result in a synergistic effect on TrOCs' removal and degradation, an exciting possibility yet to be systematically investigated. The recent development of anaerobic osmotic membrane bioreactors (AnOMBRs) with prolonged SRT (e.g., ~ 60 d) may further enable enhanced TrOCs removal, which is on top of their efficient organic carbon removal (> 96%), biogas recovery (0.21 L/g COD), and nutrient removal (nearly 100% total phosphorus and 62% ammonia-nitrogen) [35–41].

In the current study, we applied an AnOMBR for cytostatic drugs removal. To the best knowledge of the authors, this is the first study for investigating the removal mechanisms of cytostatic drugs and their impacts on the performance of AnOMBRs. Our study provides important implications to the application and operation of AnOMBRs.

2. Materials and methods

2.1. Experimental set-up and operating conditions

A laboratory-scale AnOMBR with an effective volume of 3.6 L was operated at 25 °C. The AnOMBR was equipped with temperature, conductivity, pressure, pH and oxidation-reduction potential (ORP) monitoring units (Mettler-Toledo M200 system) following our previous studies [35,37]. A flat-sheet FO membrane made of thin-film composite (TFC) polyamide (Hydration Technologies Inc.) with 0.025 m^2 was submerged in the bioreactor. The membrane was oriented with the dense active layer facing the reactor and the support side facing the draw solution. The support layer was made of polysulfone, and its thickness was approximately 47.2 μm. The influent pump was controlled by a water level sensor to maintain a constant water level in the reactor. Produced biogas was recycled with a recirculation rate of 2 L/min to mix the biomass and to alleviate membrane fouling. A 0.5 M NaCl solution was used as the draw solution (with the conductivity in a range of 45.0–45.5 mS/cm), whose concentration was maintained constant by a conductivity controller connected to a 5 M NaCl solution tank. The flow rate of draw solution was kept at 0.4 L/min to minimize the effect of external concentration polarization. The permeate flux was derived by mass balance to account for the mass of 5 M NaCl dosed into the draw solution tank, and then normalized for the membrane area. During the entire AnOMBR operation, the SRT was kept at 60 days, and the HRT was in a range of 15–40 h depending on the membrane flux.

The influent water of the AnOMBR was synthetic domestic wastewater, and its composition was summarized in Table S1. The total organic carbon (TOC), ammonia nitrogen (NH_4^+-N), total nitrogen (TN) and total phosphorus (TP) of the synthetic wastewater were 127.5 ± 12.7, 15.3 ± 1.0, 40.3 ± 1.2 and 5.3 ± 0.5 mg/L, respectively. Its conductivity and pH were 1.1 ± 0.1 mS/cm and 7 ± 0.1, respectively. The seed sludge was collected from a local wastewater treatment plant (Ulu Pandan Water Reclamation Plant, Singapore). Before the seed sludge was put into the reactor, it was cultivated in a fermentation flask with an effective volume of 5 L by the synthetic wastewater for about 30 days at the temperature of 25 ± 0.5 °C. The initial mixed liquor suspended solids (MLSS) in the AnOMBR was controlled at about 5 g/L. During the operation of the reactor, the conductivity of its mixed liquor will slowly increase. In the current study, the supernatant was discharged when the conductivity in the bioreactor reached about 20 mS/cm for controlling the salinity in the reactor, after which the FO membrane module was replaced with a new one and then a new operation cycle was started. Before adding cytostatic drugs into the bioreactor, the AnOMBR was operated for 78 days.

2.2. Cytostatic drugs addition

A group of 8 cytostatic drugs of high environmental relevance was tested in this study, including cyclophosphamide (CP), azathioprine (Aza), methotrexate (Met), doxorubicin (Dox), epirubicin (Epi), flutamide (Flu), mitotane (Mit), and tamoxifen (Tam), supplied by Sigma-Aldrich (Singapore) with high purity (≥98%). The internal standard cyclophosphamide-d_8 (CP-d_8) was obtained from TLC PharmaChem (Ontario, Canada). Individual stock solution of 1.0 g/L was prepared in HPLC-grade methanol (Merck, Singapore) and stored at −20 °C. A working solution containing 1 mg/L of each compound was then prepared in deionized water, and then dosed into the AnOMBR system at two concentration levels of 100 ng/L and 100 μg/L on days of 84 and 87, respectively. The main physicochemical properties of target compounds are summarized in Table 1. The cytostatic drugs at each concentration level were continuously added into the reactor for 3 days, and the water samples including influent water, sludge supernatant and FO permeate and sludge samples in the bioreactor were collected before and after each adding experiment.

2.3. Batch experiment design

In order to distinguish the adsorption and biodegradation of biomass for the 8 cytostatic drugs in the AnOMBR, a batch experiment was carried out simultaneously. In the batch test, five 5 L glass beakers with 3 L mixed liquor were operated simultaneously at 25 ± 0.5 °C for 48 h following the three treatments (I, II and III) summarized in Table 2. All reactors were placed in a dark chamber to avoid possible photolysis.