GEMIMA SANTOS ARCANJO

AN ANAEROBIC OSMOTIC MEMBRANE BIOREACTOR COUPLED WITH MEMBRANE DISTILLATION FOR REMOVAL OF ORGANIC MICROPOLLUTANTS AND ESTROGENIC ACTIVITY FROM MUNICIPAL SEWAGE

Tese apresentada à Universidade Federal de Viçosa, como parte das exigências do Programa de Pós-Graduação em Engenharia Civil, para obtenção do Título de *Doctor Scientiae*.

Orientadora: Ann Honor Mounteer
Coorientadora: Míriam Cristina Santos Amaral Moravia

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À minha amada família, por ser minha fortaleza, dedico!

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ABSTRACT

ARCANJO, Gemima Santos, D.Sc., Universidade Federal de Viçosa, June, 2021. **An anaerobic osmotic membrane bioreactor coupled with membrane distillation for removal of organic micropollutants and estrogenic activity from municipal sewage**. Adviser: Ann Honor Mounteer. Co-adviser: Míriam Cristina Santos Amaral Moravia.

The contamination of water sources by pharmaceutically active compounds (PhACs) and their effect on aquatic communities and human health have become an environmental concern worldwide. Municipal sewage is the major source of organic micropollutants in the environment. Even when there is a sewage treatment plant present, conventional biological treatment cannot remove recalcitrant compounds. Membrane bioreactors (MBRs), due to their high solids concentrations and retention times, improve biological treatment removal of nutrients and recalcitrant organic compounds. Forward osmosis (FO) and membrane distillation (MD), which present high rejection of dissolved compounds, even at concentrations of $\mu g\ L^{-1}$ and $ng\ L^{-1}$, are an alternative for use in MBRs treating municipal sewage. Thus, this research aimed to evaluate the performance of an anaerobic osmotic membrane bioreactor coupled with membrane distillation (AnOMBR-MD) in treatment of municipal sewage containing PhACs (17α- ethinylestradiol, betamethasone, ketoprofen, fenofibrate, fluconazole, loratadine e prednisone). The AnOMBR-MD was operated with NaCl as draw solute in a hybrid submerged FO-MD module. The removal efficiencies of dissolved organic carbon (DOC) and $P\text{-}PO_4^{3-}$ were 97.2% and 98.0%. $N\text{-}NH_4^+$ accumulated in the bioreactor and reached the draw solution (DS) and distillate. Changes in the microbial community were observed due to salinity build-up and the presence of PhACs, while the system removed more than 96.4% of the compounds evaluated. Estrogenic activity was not detected in distillate samples and the environmental and human health risks sharply declined. A second study was conducted to select the best DS salt in the integrated FO-MD hybrid module. The technique to order preference by similarity to the ideal solution was used in in multicriteria decision making, that considered results of water and salt flux, energy consumption, costs, and FO and global rejection of micropollutants for each draw solute tested (NaCl, $MgCl_2$, sodium acetate (NaOAc), magnesium acetate ($MgOAc_2$), and EDTA-Na_2). $MgCl_2$ was selected as the best salt for the DS in the FO-MD system and could be used to mitigate salinity build-up in the mixed liquor, followed in order of rank by NaCl, NaOAc, EDTA-Na_2 and $MgOAc_2$. In the third study, $MgCl_2$ was used as draw solute of the AnOMBR-MD in treatment of synthetic municipal sewage containing PhACs and estrogenic

activity. Due to organic and inorganic fouling, permeate fluxes declined 82 and 67%, for FO and MD, respectively. MD salt rejection was higher than 99.6% and more than 90% of dissolved organic carbon was removed. P-PO_4^{3-} rejection by the FO-MD module was greater than 99.98%, which led to accumulation of this nutrient in the mixed liquor (ML). N-NH_4^+ concentration in the ML also increased, and with the reverse flux of Mg^{2+}, precipitation of struvite, magnesite and monetite may have occurred. Salinity build-up was lower than when NaCl was used as DS. The ML conductivity increased until day 21 and then stabilized. Biological removal of estrogenic activity was reduced with salt accumulation, but increased after salinity stabilization. AnOMBR-MD removal of estrogenic activity was higher than 99.97%, with reduction in environmental and non-carcinogenic human risks from high to low, while incremental lifetime carcinogenic risk decreased to negligible. On the other hand, risk assessment showed that a better removal of ketoprofen and loratadine is needed, since the acute environmental risk of the distillate was still high, due to the presence of these substances. The results of the present research demonstrated that permeate fluxes in FO and MD are still low and some strategies to overcome this drawback are needed, such as physical and chemical cleaning. Furthermore, the use of the YES assay combined with detection and identification of micropollutants allowed an effective assessment of overall treatment performance.

Keywords: Microbial community. Concentration polarization. Reverse salt flux. YES assay. Risk assessment.

RESUMO

ARCANJO, Gemima Santos, D.Sc., Universidade Federal de Viçosa, junho de 2021. **Remoção de micropoluentes orgânicos e atividade estrogênica de esgoto doméstico em um biorreator osmótico anaeróbio acoplado à destilação com membranas**. Orientadora: Ann Honor Mounteer. Coorientadora: Míriam Cristina Santos Amaral Moravia.

A contaminação dos recursos hídricos por fármacos (PhACs) e os seus efeitos em organismos aquáticos e aos seres humanos tornou-se um problema de grande preocupação ambiental. Esgotos domésticos são a principal fonte de micropoluentes orgânicos para o meio ambiente. Mesmo quando existem estações de tratamento de esgotos, o tratamento biológico convencional não é capaz de remover compostos recalcitrantes. Biorreatores com membranas (MBRs), por permitirem elevada concentração de sólidos e maior tempo de residência celular, apresentam maior eficiência na remoção de nutrientes e compostos orgânicos recalcitrantes. O uso de membranas de osmose direta (FO) e de destilação (MD), que apresentam elevada rejeição de compostos dissolvidos, mesmo em concentrações de $\mu g\ L^{-1}$ e $ng\ L^{-1}$, pode ser uma alternativa para MBRs no tratamento de esgoto doméstico. Desta forma, esta pesquisa teve como objetivo avaliar o desempenho de um biorreator osmótico anaeróbio acoplado à destilação com membranas (AnOMBR-MD) no tratamento de esgoto doméstico contendo PhACs (17α-etinilestradiol, betametasona, cetoprofeno, fenofibrato, fluconazol, loratadina e prednisona). O AnOMBR-MD foi operado utilizando NaCl como o soluto da solução osmótica (DS) do módulo híbrido submerso de FO-MD. A eficiência de remoção de carbono orgânico dissolvido (DOC) e $P\text{-}PO_4^{3-}$ foi de 97,2% e 98,0%. Em relação ao $N\text{-}NH_4^+$, foi observado o acúmulo no biorreator, atingindo a DS e o destilado. Mudanças na comunidade microbiana foram observadas devido ao acúmulo de salinidade e à presença de PhACs, enquanto o sistema removeu mais de 96,4% dos compostos avaliados. A atividade estrogênica não foi detectada em amostras de destilados e os riscos ambientais e para a saúde humana foram reduzidos. Um segundo estudo foi conduzido para selecionar o melhor soluto para a DS no módulo híbrido de FO-MD. A técnica para avaliar o desempenho das alternativas através da similaridade com a solução ideal foi utilizada para auxiliar na tomada de decisão, considerando os resultados de fluxo de água e sal, consumo de energia, custos e rejeição na FO e global de micropoluentes, para cada soluto testado (NaCl, $MgCl_2$, acetato de sódio (NaOAc), acetato de magnésio ($MgOAc_2$) e EDTA-Na_2). O $MgCl_2$ foi selecionado como o melhor sal para o sistema de FO-MD e pode ser usado para mitigar o acúmulo de salinidade no líquido reacional, seguido em ordem de classificação

por NaCl, NaOAc, EDTA-Na_2 e $MgOAc_2$. No terceiro estudo, $MgCl_2$ foi utilizado para compor a DS do AnOMBR-MD no tratamento de esgoto doméstico sintético, contendo PhACs e atividade estrogênica. Devido à incrustação orgânica e inorgânica, os fluxos de permeado reduziram 82 e 67%, para FO e MD, respectivamente. A rejeição do sal pela MD foi superior a 99,6% e mais de 90% do carbono orgânico dissolvido foi removido. A rejeição de $P\text{-}PO_4^{3-}$ pelo módulo FO-MD foi superior a 99,98%, o que promoveu o acúmulo desse nutriente no líquido reacional (ML). A concentração de $N\text{-}NH_4^+$ no ML também aumentou, e com o fluxo inverso de sal de Mg^{2+}, pode ter ocorrido a precipitação de estruvita, magnesita e monetita. O acúmulo de salinidade foi menor do que na operação com NaCl. A condutividade do ML aumentou até o dia 21 e depois se estabilizou. A remoção biológica de atividade estrogênica diminuiu com o acúmulo de sal, mas aumentou novamente após a estabilização da salinidade. A remoção da atividade estrogênica pelo AnOMBR-MD foi superior a 99,97%, o que levou à redução nos riscos ambiental e humano não carcinogênico de alto para baixo, enquanto o incremento de risco carcinogênico ao longo da vida diminuiu para desprezível. Por outro lado, a avaliação de risco mostrou que uma melhor remoção de cetoprofeno e loratadina é necessária, uma vez que o risco ambiental agudo do destilado ainda era alto, devido à presença desses fármacos. Os resultados da presente pesquisa demonstraram que os fluxos de permeado em FO e MD ainda são baixos e algumas estratégias para contornar esta desvantagem são necessárias, como limpeza física e, ou química. Além disso, o uso do ensaio YES combinado com a detecção e identificação de micropoluentes permitiu uma avaliação eficaz do desempenho geral do tratamento.

Palavras-chave: Comunidade microbiana. Polarização da concentração. Fluxo inverso de sal. Ensaio YES. Avaliação de risco.

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LIST OF ABBREVIATIONS, ACRONYMS AND SIMBOLS

A	Water permeability coefficient
AL-FS	Active layer facing the feed solution
A_m	Membrane area
AnOMBR	Anaerobic osmotic membrane bioreactor
AnOMBR-MD	Anaerobic osmotic membrane bioreactor – membrane distillation
AT	Average time
B	Salt permeability coefficient
BET	Betamethasone
BW	Body weight
C_{DS}	Contaminant concentration in the draw solution
$C_{DS,MD}$	Draw solution concentration at membrane distillation surface
C_{FS}	Contaminant concentration in the feed solution
C_{ML}	Contaminant concentration in the mixed liquor
C_{MLSS}	Mixed liquor total suspended solids
COD	Chemical oxygen demand
$C_{p,MD}$	Contaminant concentration in the distillate
CPRG	Chlorophenol red-b-D-galactospyranoside
CSF	Cancer slope factor
C_{Slg}	Contaminant concentration in the sludge phase
CTA	Cellulose triacetate
D	Diffusion coefficient
DI	Daily input
DNA	Deoxyribonucleic acid
DOC	Dissolved organic carbon
DS	Draw solution
DWGL	Drinking water guideline level
E2-eq	Estrogenic activity reported as estradiol equivalents
EC	Electrical conductivity
EC50	Effect concentration
ECP	External concentration polarization
ED	Exposure duration
EDCs	Endocrine disrupting compounds
EDX	Energy dispersive spectroscopy

EE2	17α-ethinylestradiol
EF	Exposure frequency
EPS	Extracellular polymeric substances
FEF	Flux efficiency factor
FEN	Fenofibrate
FLU	Fluconazole
FO	Forward osmosis
FS	Feed solution
hERα	Human estrogen receptor
HI	Hazard index
HQ	Hazard quotient
HQ_h	Human health risk
HRT	Hydraulic retention time
ICP	Internal concentration polarization
ILCR	Incremental lifetime carcinogenic risk
J_{FO}	Forward osmosis water flux
J_{MD}	Membrane distillation water flux
J_s	Reverse salt flux in forward osmosis membrane
J_{sMD}	Salt flux in membrane distillation
KET	Ketoprofen
$k_{F,FO}$	Mass transfer coefficient on the feed solution side of FO membrane
$k_{m,FO}$	Mass transfer coefficient within the FO membrane support layer
K_{ow}	Octanol/water partition coefficient
LC50	Letal concentration
LC-MS	Liquid-chromatography coupled with mass spectrometry
LOR	Loratadine
M_{bio}	Contaminant mass removed due to biological process
M_{biodeg}	Contaminant mass removed due to biodegradation
$M_{biosorp}$	Contaminant mass removed due to biosorption onto the sludge
MBR	Membrane bioreactor
MD	Membrane distillation
MEC	Measured concentration
MF	Microfiltration
ML	Mixed liquor
MLVSS	Mixed liquor volatile suspended solids

n	Number of species that the draw solute dissociates into
NOEC	No observed effect concentration
OMBR	Osmotic membrane bioreactor
P_{DS}	Vapor pressure in bulk draw solution
$P_{DS,m}$	Vapor pressure at MD feed surface
PhACs	Pharmaceutically active compounds
PNEC	Predicted non-effect concentration
PRE	Prednisone
PTFE	Polytetrafluoroethylene
R	Gas constant
R_{AnOMBR}	Removal efficiency of the bioreactor combined with FO rejection
$R_{AnOMBR-MD}$	Overall removal efficiency of the AnOMBR-MD
R_{bio}	Biological removal
R_{biodeg}	Biological removal due to biodegradation
$R_{biosorp}$	Biological removal due to biosorption onto the sludge
R_{FO}	Rejection by the FO membrane
R_{FO-MD}	Rejection by the hybrid FO-MD module
R_g	Global rejection
RP	Relative potency
RQ	Environmental risk quotient
RQac	Acute environmental risk quotient
RQch	Chronic environmental risk quotient
$R_{salt,MD}$	Membrane distillation salt rejection
S	Structural parameter
SEC_{pump}	Specific energy consumption for pumping
SEM	Scanning electron microscopy
SMP	Soluble microbial products
SPE	Solid phase extraction
SRB	Sulfate-reducing bacteria
SRT	Solids residence time
STPs	Municipal sewage treatment plants
T	Temperature
TDI	Tolerable daily intake
TOPSIS	Technique for order preference by similarity to ideal solution
TrOC	Trace organic compounds

TSS	Total suspended solids
UASB	Upflow Anaerobic Sludge Blanket
UF	Ultrafiltration membrane
VFA	Volatile fatty acids
V_{FS}	Volume of the feed solution entering the bioreactor
V_R	Bioreactor volume
VSS	Volatile suspended solids
V_{Wslg}	Volume of waste sludge discharged
WWTPs	Wastewater treatment plants
YES	Yeast estrogenic screen
ΔP_v	Vapor pressure difference
$\Delta\pi$	Osmotic pressure difference
$\Delta\pi_b$	Bulk osmotic pressure gradient
$\Delta\pi_{eff}$	Osmotic pressure difference across the active layer of the FO membrane
ζ	Concentration polarization coefficient
$\pi_{DS,b}$	Osmotic pressure of the draw solution
$\pi_{DS,i}$	Osmotic pressure of the draw solution at the membrane interface
$\pi_{f,b}$	Osmotic pressure of the feed solution
$\pi_{f,i}$	Osmotic pressure of the feed solution at the feed-membrane interface
τ	Temperature polarization coefficient
ψ	Vapor pressure polarization coefficient

SUMMARY

1 General introduction

The release of toxic compounds in the aquatic environment is of great concern worldwide. Pharmaceutically active compounds (PhACs) are recalcitrant and biologically active substances receiving much attention because of their high consumption and continuous release into the environment [1]. Some PhACs are also classified as endocrine disruptors chemicals (EDCs), which are defined as exogenous substances or mixtures that can alter the function of the endocrine system of animals [2]. Estrogenic compounds are EDCs that affect the processes linked to reproduction and development [3].

Once ingested, a large part of PhACs is not metabolized and are released to the municipal sewage system. Conventional sewage treatment plants (STPs) are projected to remove organic pollutants and nutrients and are not effective in removing recalcitrant PhACs [4]. Thus, it is necessary to investigate new ways of reducing the concentrations of these compounds in treated sewage and thereby reduced their risk to the environment and human health.

Membrane bioreactors (MBRs) combine biological treatment and membrane separation processes [5]. MBRs gained attention since they allow higher solids concentration and solid retention time, which can increase performance of the biological process [6]. The development of osmotic membrane bioreactors (OMBRs) that integrate the forward osmosis (FO) process into the MBR, improves reactor efficiency through rejection of dissolved compounds, such as organic micropollutants, trace metals and nutrients [7]. The driving force is the osmotic pressure difference between the draw solution (DS) and the bioreactor. Since hydraulic pressure is not needed, energy consumption and membrane fouling are reduced, when compared with conventional MBRs [8]. The challenges in OMBR operation are salt accumulation and the need for an additional process to recover the purified water from the DS and maintain the osmotic pressure gradient [9].

Membrane distillation (MD) is a separation process that uses a microporous and hydrophobic membrane, which allows the passage of water vapor and volatile compounds, due to the vapor pressure difference across the membrane. MD has been used to reconcentrate DS, rejecting more than 99% of the draw solute [8,10,11]. The integration of OMBR with MD could be advantageous for the treatment of municipal sewage. Recent studies have reported that OMBR-MD can reach micropollutants removal efficiencies of more than 96% [11,12].

Proper selection of DS salt is very important for OMBRs performance since, undesirable reverse salt flux (J_s) will depend on salt diffusivity. Reverse flux from the DS to the bioreactor must be controlled to reduce salinity build-up that reduces the osmotic pressure gradient and affects microbial activity [13]. Solute costs, solubility and osmotic pressure generated must also be considered [9,14].

An anaerobic OMBR coupled with MD would also reduce operational costs, since no aeration is needed, sludge production is lower than in an aerobic reactor and biogas recovery is possible [15]. Also, higher micropollutants removal efficiency is expected, when compared with conventional anaerobic treatment, since these compounds have a longer residence time, allowing their biodegradation [16].

Therefore, it is important to evaluate the performance of an AnOMBR-MD in treatment of municipal sewage containing PhACs and estrogenic compounds. Furthermore, the performance of different salts as draw solute in a hybrid FO-MD module should be investigated, taking into consideration costs, reverse salt and, permeate fluxes and effects on micropollutants removal.

This document is composed of three chapters. The first chapter reports on the estrogenicity of seven PhACs and evaluates the removal of PhACs and estrogenic activity from municipal sewage treated in an AnOMBR-MD operated with NaCl as DS. In the second chapter, use of five draw solutes (NaCl, $MgCl_2$, sodium acetate, magnesium acetate and EDTA-Na_2) are compared in a submerged FO-MD module. TOPSIS (technique for order preference by similarity to ideal solution) is used in multicriteria decision making to select the best solute. The third chapter evaluates the use of $MgCl_2$, chosen as the best solute in chapter 2, as draw solute in the AnOMBR-MD, for treatment of synthetic municipal sewage containing PhACs. Environmental and human health risks are also assessed.

References

[1] B. Tiwari, B. Sellamuthu, Y. Ouarda, P. Drogui, R.D. Tyagi, G. Buelna, Review on fate and mechanism of removal of pharmaceutical pollutants from wastewater using biological approach, Bioresource Technology. 224 (2017) 1–12. https://doi.org/10.1016/j.biortech.2016.11.042.

[2] WHO, WHO | State of the science of endocrine disrupting chemicals - 2012, (2012). http://www.who.int/ceh/publications/endocrine/en/ (accessed August 19, 2017).

[3] L. Griffero, G. Gomes, M. Berazategui, C. Fosalba, F. Teixeira de Mello, C.E. Rezende, D.M. Bila, J. García-Alonso, Estrogenicity and cytotoxicity of sediments and water from the drinkwater source-basin of Montevideo city, Uruguay, Ecotoxicology and Environmental Contamination. 13 (2018) 15–22. https://doi.org/10.5132/eec.2018.01.02.

[4] S.F. de Aquino, E.M.F. Brandt, C.A. de L. Chernicharo, Remoção de fármacos e desreguladores endócrinos em estações de tratamento de esgoto: revisão da literatura, Engenharia Sanitária e Ambiental. 18 (2013) 187–204. https://doi.org/10.1590/S1413-41522013000300002.

[5] S. Judd, C. Judd, The MBR book: principles and applications of membrane bioreactors in water and wastewater treatment, 1st ed, Elsevier, Amsterdam ; Boston, 2006.

[6] S.K. Maeng, B.G. Choi, K.T. Lee, K.G. Song, Influences of solid retention time, nitrification and microbial activity on the attenuation of pharmaceuticals and estrogens in membrane bioreactors, Water Research. 47 (2013) 3151–3162. https://doi.org/10.1016/j.watres.2013.03.014.

[7] R.W. Holloway, A. Achilli, T.Y. Cath, The osmotic membrane bioreactor: a critical review, Environmental Science: Water Research & Technology. 1 (2015) 581–605. https://doi.org/10.1039/C5EW00103J.

[8] H.-M. Chang, S.-S. Chen, N.C. Nguyen, W.-S. Chang, S. Sinha Ray, Osmosis membrane bioreactor–microfiltration with magnesium-based draw solute for salinity reduction and phosphorus recovery, International Biodeterioration & Biodegradation. 124 (2017) 169–175. https://doi.org/10.1016/j.ibiod.2017.05.022.

[9] D.J. Johnson, W.A. Suwaileh, A.W. Mohammed, N. Hilal, Osmotic's potential: An overview of draw solutes for forward osmosis, Desalination. 434 (2018) 100–120. https://doi.org/10.1016/j.desal.2017.09.017.

[10] N. Cong Nguyen, H. Cong Duong, S.-S. Chen, H. Thi Nguyen, H. Hao Ngo, W. Guo, H. Quang Le, C. Cong Duong, L. Thuy Trang, A. Hoang Le, X. Thanh Bui, P. Dan Nguyen, Water and nutrient recovery by a novel moving sponge – Anaerobic osmotic membrane bioreactor – Membrane distillation (AnOMBR-MD) closed-loop system, Bioresource Technology. 312 (2020) 123573. https://doi.org/10.1016/j.biortech.2020.123573.

[11] B.C. Ricci, G.S. Arcanjo, V.R. Moreira, Y.A.R. Lebron, K. Koch, F.C.R. Costa, B.P. Ferreira, F.C. Lisboa, L.D. Miranda, C.V. de Faria, L.C. Lange, M. Amaral, A novel submerged anaerobic osmotic membrane bioreactor coupled to membrane distillation for water reclamation from municipal wastewater, Chemical Engineering Journal. (2021) 128645. https://doi.org/10.1016/j.cej.2021.128645.

[12] Y. Kim, S. Li, L. Chekli, Y.C. Woo, C.-H. Wei, S. Phuntsho, N. Ghaffour, T. Leiknes, H.K. Shon, Assessing the removal of organic micro-pollutants from anaerobic membrane bioreactor effluent by fertilizer-drawn forward osmosis, Journal of Membrane Science. 533 (2017) 84–95. https://doi.org/10.1016/j.memsci.2017.03.027.

[13] G. Qiu, Y.-P. Ting, Osmotic membrane bioreactor for wastewater treatment and the effect of salt accumulation on system performance and microbial community dynamics, Bioresource Technology. 150 (2013) 287–297. https://doi.org/10.1016/j.biortech.2013.09.090.

[14] Y. Cai, X. ‘Matthew’ Hu, A critical review on draw solutes development for forward osmosis, Desalination. 391 (2016) 16–29. https://doi.org/10.1016/j.desal.2016.03.021.

[15] T. Stephenson, K. Brindle, S. Judd, B. Jefferson, Membrane Bioreactors for Wastewater Treatment, 1st ed., IWA Publishing, London, UK, 2000.

[16] G. Qiu, S. Zhang, D.S. Srinivasa Raghavan, S. Das, Y.-P. Ting, The potential of hybrid forward osmosis membrane bioreactor (FOMBR) processes in achieving high throughput treatment of municipal wastewater with enhanced phosphorus recovery, Water Research. 105 (2016) 370–382. https://doi.org/10.1016/j.watres.2016.09.017.

2 Objectives

The general objective was to evaluate the AnOMBR-MD performance treating municipal sewage containing pharmaceutical active compounds.

The specific objectives were:

- To investigate the removal of seven selected PhACs and estrogenic activity from municipal sewage by an AnOMBR-MD operated with NaCl as draw solute;
- To assess the microbial community change due to salinity build-up in the AnOMBR-MD;
- To evaluate the effect of five different salts in a FO-MD integrated in a submerged hybrid module concerning PhACs rejections;
- To evaluate the removal of seven selected PhACs and estrogenic activity from synthetic municipal sewage by an AnOMBR-MD operated with $MgCl_2$ as draw solute;
- To evaluate the effect of salinity build-up on biological removal of estrogenic activity by an AnOMBR-MD operated with $MgCl_2$ as draw solute;
- To assess environmental and human health risks reduction from a municipal sewage by an AnOMBR-MD;

Chapter 1: Effective removal of pharmaceutical compounds and estrogenic activity by a hybrid anaerobic osmotic membrane bioreactor – membrane distillation system treating municipal sewage

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Effective removal of pharmaceutical compounds and estrogenic activity by a hybrid anaerobic osmotic membrane bioreactor – Membrane distillation system treating municipal sewage

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Abstract: Pharmaceutically active compounds (PhACs) may cause harmful effects in living beings, and advanced treatment is required to improve wastewater treatment plant efficiency. In this context, this study aimed to assess the performance of a hybrid anaerobic osmotic membrane bioreactor coupled with a membrane distillation system (AnOMBR-MD) for removing PhACs and estrogenic activity from municipal sewage. Human health and environmental risks of produced water were also assessed. The removal efficiency of dissolved organic carbon and $P\text{-}PO_4^{3-}$ reached 97.2% and 98.0%, respectively. $N\text{-}NH_4^+$ accumulated in the bioreactor since anaerobic treatment can not remove it. Salinity increase in the bioreactor caused a great change in the microbial community, with Chao 1 and Shannon indexes higher in the sludge after 50 days of operation than in the sludge used as inoculum. Estrogenic activity of municipal sewage spiked with PhACs was more than 3 times higher than the expected value calculated by the additive model (2 $\mu g\ L^{-1}$E2-eq.), which indicates that some of the PhACs effects increased in the presence of others. Estrogenicity was not detected in distillate samples, which greatly reduced human health risks to acceptable values. Of the 7 PhACs selected in this study, only betamethasone, fluconazole, and prednisone were detected in the distillate. However, the overall removal of PhACs by the AnOMBR-MD system was higher than 96.4%. The chronic environmental risk considering the estrogenic activity was classified as high because of the detection limit in the yeast estrogen screen (YES), which supports the need for improving bioassay sensibility. The results demonstrated that the use of the YES assay combined with detection and identification of micropollutants allowed an effective assessment of the overall treatment performance.

Keywords: micropollutants; YES assay; microbial community; sewage treatment; risk assessment.

1 Introduction

The presence of pharmaceutically active compounds (PhACs) in the environment has attracted increasing attention due to their continuous discharge, persistence, and biological activity, which may cause disturbances in aquatic flora and fauna and risks to human health [1]. Over 3,000 different PhACs are in use worldwide, and it has been reported to be increasing because of population growth and aging [2].

Some PhACs are classified as endocrine-disrupting compounds (EDCs), defined as agents that alter endocrine system functions, such as secretion, transport, synthesis, binding, and elimination of natural hormones, even at concentrations in the range of ng L^{-1} [3]. A group of EDCs that gets much attention is the estrogenic substances that act in the same way as the natural female hormone 17β-estradiol [4]. The synthetic hormone 17α-ethinylestradiol, used in birth control pills, has an estrogenic potency equal to or higher than 17β-estradiol [5]. Other than synthetic and natural hormones, phenolic compounds, like nonylphenol, and phthalates esters, such as dibutyl phthalate, may also mimic 17β-estradiol activity [4]. In most cases, EDCs are much less potent than 17β-estradiol, ranging from one-thirtieth to one ten-thousandth as active [6]. Some of the effects associated with EDCs are feminization of male fish and turtles, changes in the immunologic system of marine mammals; and in humans, reduction of sperm production, increase in the incidence of breast, testicle, and prostate cancers, precocious puberty, polycystic ovary syndrome and premature ovarian failure [4].

Nonetheless, most of the studies reported in the literature use analytical chemistry methods to detect and quantify micropollutants in environmental samples and to evaluate the efficiency of water and wastewater treatment technologies [7–10]. They are essential to understand the route of compounds; however, a priori knowledge about these compounds is required and it is not possible to analyze all the substances present in the different environmental compartments [11]. Also, some PhACs may have endocrine-disrupting effects at concentrations below their analytical limits of detection [12]. And even if the compound is detected and its concentration is below the one with no observed effect, the mixture of more than one micropollutant may have interactions such as synergism, antagonism and additivity [13].

Therefore, the use of bioanalytical tools, such as *in vitro* assays, is crucial to assess the biological activity of waters and wastewaters since they are complex mixtures of compounds, including EDCs [12]. *In vitro* assays are also less expensive and ethically more acceptable than

in vivo alternatives [14]. However, for some compounds, bioassays are less sensitive than analytical investigation techniques [15].

Although *in vitro* estrogenic assays cannot predict real hazards to the whole organism and population, they allow for rapid screening of estrogen mimetic potential of samples of unknown composition [12]. The YES (yeast estrogenic screen) assay, developed by Routledge and Sumpter [16], utilizes a recombinant strain of the yeast *Saccharomyces cerevisiae* modified with the human estrogen receptor (hERα). It is one of the most frequently used *in vitro* bioassays to detect and quantify the potential estrogenicity of compounds, waters, and sewage.

Municipal sewage treatment plants (STPs) are designed to remove easily or moderately biodegradable carbon, nutrients, and microorganisms and, therefore, do not efficiently reduce micropollutant concentrations [17]. Therefore, to improve the removal efficiency, advanced treatment technologies, such as membrane separation processes, are required.

Osmotic membrane bioreactors (OMBRs) have been successfully applied in pilot and lab-scale for wastewater treatment, since they have a low energy consumption and fouling tendency when compared to conventional membrane bioreactors (MBRs) [18,19]. Furthermore, the forward osmosis (FO) membrane used in OMBRs presents better retention of low molecular weight compounds [10]. The water permeates through the FO membrane from the feed solution to the draw solution (DS), which has a higher osmotic pressure [20].

Anaerobic MBRs (AnMBRs) have advantages over aerobic MBRs that include lower operating costs because there is no need for aeration, less sludge production, and they offer the possibility of energy recovery in the form of biogas [21]. However, anaerobic treatment is known to have lower organic matter, nutrients, and micropollutant removal efficiency, when compared to aerobic processes [22]. In an AnOMBR, this disadvantage is overcome since the FO membrane increases contaminant retention times sufficiently to allow their biodegradation [23]. For example, in an AnOMBR, the FO rejection of caffeine, atenolol and atrazine was equal to 93.1%, 99.6%, and 93.3%, respectively [10], while in an AnMBR with an ultrafiltration membrane (UF), caffeine and atenolol were not removed, and atrazine was only reduced by 20% [9].

In order to maintain the osmotic pressure difference ($\Delta\pi$), which is the driving force in FO, and to recover the produced water, a subsequent separation and purification process is needed. Membrane distillation (MD) has been reported as a regeneration process for FO draw solution, with salt rejection higher than 99.7% [24]. The water vapor passes through the

membrane due to the vapor pressure gradient generated by the temperature difference across the microporous and hydrophobic membrane. The vapor condenses on the distillate side, while non-volatile compounds are rejected by the membrane [25]. Thus, integration of AnOMBR with MD (AnOMBR-MD) has a great potential for treating wastewaters containing micropollutants to produce high quality permeate for even potable reuse. Ricci et al. [24] proposed a novel submerged hybrid FO-MD module for domestic sewage treatment and found over 97.5% rejection of PhACs.

Reverse salt flux (J_s) is one of the drawbacks of OMBRs. Because of the higher solute concentration difference between the DS and the bioreactor, to guarantee osmotic pressure difference, salt diffusion occurs from the DS to the mixed liquor [20]. Due to the great salt rejection by the FO membrane and Js, salt accumulation in the bioreactor affects the microbial community, thus influencing the biological removal of organic matter, nutrients, and micropollutants [26].

The objectives of this study were to investigate the removal of 7 selected PhACs and estrogenic activity from municipal sewage by an anaerobic osmotic membrane bioreactor integrated with membrane distillation. Microbial community change due to salinity build-up and environmental, human health, and cancer risks of the produced water were also assessed. This is the first paper to assess the human health and environmental risks in an AnOMBR-MD, based on both estrogenicity and PhACs concentration.

2 Material and methods

2.1 *Chemicals and municipal sewage feed*

Seven compounds were chosen as PhACs for the AnOMBR-MD operation: 17α-ethinylestradiol, betamethasone, fenofibrate, fluconazole, ketoprofen, loratadine, and prednisone. All have been found in domestic sewage, surface, ground, and drinking water in Brazil [27–29]. The 7 PhACs were purchased from Sigma Aldrich (Cotia, São Paulo, Brazil), and stock solutions (2 mg L^{-1}) of each were prepared in pure methanol (Sigma Aldrich) and stored at -20 °C until used. Individual solutions were prepared in HPLC grade ethanol (Honeywell, North Carolina, USA) and stored at -20 °C until used to evaluate the estrogenic activity of each PhAC. Physicochemical properties of the 7 PhACs are presented in Table 1. For the YES assay, 17β-estradiol (Sigma Aldrich, Cotia, São Paulo, Brazil) was used to prepare

the standard curve in HPLC grade ethanol at a concentration of 54.5 μg L^{-1}. Chlorophenol red-b-D-galactospyranoside (CPRG) was purchased from Merck Millipore (Barueri, São Paulo, Brazil).

Table 1 - Physicochemical properties of PhACs used in the study

PhACs	MW (g mol^{-1})	Log K_{ow}	pK_a	pK_H	DL_{dist} (ng L^{-1})	DL_{DS} (ng L^{-1})
17α-Ethynilestradiol	296.41	3.9	-1.66 and 10.33	11.09	83.6	708.7
Betamethasone	392.47	1.68	12.42	7.14	3.3	28.3
Fenofibrate	306.27	3.61	3.88	8.34	1.1	102.8
Fluconazole	360.83	5.28	-	12.98	0.5	27.7
Ketoprofen	254.28	0.56	2.3 and 12.68	10.67	0.8	68.9
Loratadine	382.89	4.55	4.33	12.49	0.7	20.1
Prednisone	358.43	1.66	12.68	9.54	1.3	59.6

DL_{dist} - Detection limit for distillate; DL_{DS} - Detection limit for draw solution.
Source: Ricci et al. [24].

Municipal sewage was collected once after preliminary treatment, composed of screens and grit chambers, from the Onça municipal STP, located in Belo Horizonte, Minas Gerais, Brazil. Physicochemical characterization of the wastewater is presented in Table 2. Anaerobic sludge from a UASB unit was also collected once, at the same treatment plant and used as inoculum to start the operation of the AnOMBR-MD. Municipal sewage was storage under refrigeration at 4 °C until used and anaerobic sludge was fed with municipal sewage every day until the bioreactor operation started.

Table 2 - Physicochemical characterization of the municipal sewage after preliminary treatment

Parameter	**Value ± standard deviation (n = 7)**
pH	8.2 ± 0.7
Electrical conductivity (μS cm^{-1})	1608 ± 89.1
Alkalinity ($mgCaCO_3$ L^{-1})	116.5 ± 24.6
Chemical oxygen demand (COD) (mg L^{-1})	306 ± 138
Total suspended solids (TSS) (mg L^{-1})	130.1 ± 57.9
Volatile suspended solids (VSS) (mg L^{-1})	116.0 ± 43.9
Dissolved organic carbon (DOC) (mg L^{-1})	56.0 ± 16.3
$N\text{-}NH_4^+$ (mg L^{-1})	25.5 ± 8.2
$P\text{-}PO_4^{3-}$ (mg L^{-1})	6.2 ± 0.9
Estrogenic activity (E2-eq. ng L^{-1})	9.2

2.2 Membranes

Flat-sheet membranes were used in the FO-MD hybrid module. The asymmetric FO membrane, made with cellulose triacetate, was purchased from Hydration Technology Innovations (Albany, OR, USA). The FO membrane was used with the active layer facing the feed solution. For MD, a polytetrafluoroethylene (PTFE) laminated on a polypropylene layer membrane was purchased from Sterlitech Corporation (Kent, WA, USA). The MD membrane had an average pore size of 0.2 μm and was tested in direct contact configuration.

2.3 Experimental apparatus and AnOMBR-MD operation

A schematic of the lab-scale AnOMBR-MD system is shown in Figure 1. The bioreactor had an effective volume of 4.5 L and was equipped with the submerged FO-MD hybrid module and a mechanical stirrer to allow complete mixing conditions. The module has 2 FO and 2 MD membranes. Each membrane had an effective area of 132 cm^2, so the total membrane area is 264 cm^2. A detailed description of the module can be found in Ricci et al. [24]. The bioreactor also had a level sensor that activated a metering pump connected to a feed tank when the mixed liquor level decreased below a minimum. The FO-MD module had two outer compartments for DS recirculation (75 L h^{-1}) and an inner compartment for distillate recirculation (80 L h^{-1}).

Temperatures of the DS and distillate were held constant at 45 °C and 20 °C, respectively [24]. DS and distillate reservoirs were placed on digital scales to measure weight changes during operation and, thus, calculate FO and MD water fluxes.

The bioreactor was inoculated with anaerobic sludge to a final MLVSS concentration of 10 g L^{-1} and redox potential varied from -279 to -122 mV, indicating and anaerobic condition [30]. Municipal sewage spiked with 2 µg L^{-1} of each PhAC was used as feed solution for the bioreactor. DS was prepared with 2 mol L^{-1} NaCl, with an osmotic pressure of 106.7 bar at 45 °C. Bioreactor operation started with 6 L of DS and 3 L of deionized water as distillate. The AnOMBR-MD was operated under continuous flow, and samples were collected to measure physicochemical parameters, PhACs quantification, and estrogenic activity evaluation. Every day, 100 mL of the mixed liquor were collected to maintain the solids retention time in 45 days.

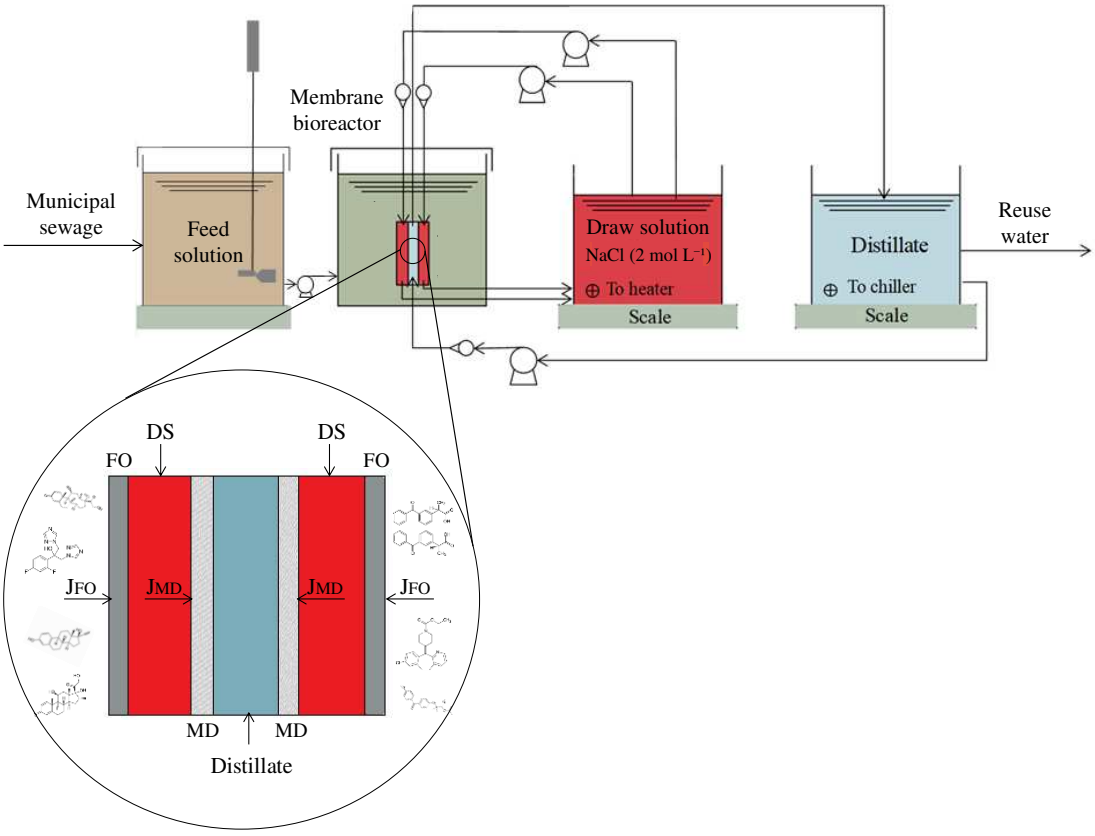

Figure 1 - Schematic of the lab-scale AnOMBR-MD system and FO-MD module.

2.4 Analytical methods

The samples were characterized by quantifying pH (4500-H^+), COD (5220 C), DOC (5310 B, Shimadzu TOC-VCPH analyzer), alkalinity (2320 B), electrical conductivity (2510), N-NH_4^+ (4500-NH_3 B and C), P-PO_4^{3-} (4500-P C) and oxidation-reduction potential (2580 A) according to the Standard Methods for the Examination of Water and Wastewater [31]. Volatile fatty acids (VFA) were quantified by the method proposed by Kapp [32].

PhACs were quantified by liquid-chromatography (Shimadzu Prominence UFLC, Shimadzu, Kyoto, Japan) coupled with mass spectrometry (MicrOTOF-QII, Bruket Daltonics, Bremen, Germany) (LC-MS). The method used to quantify the PhACs is described in detail in Ricci et al. [24] and Faria et al. [33], including recoveries and detection limits.

2.5 Molecular biology assays

One biomass sample was taken from the seeding sludge and from mixed liquor at steady state (50 d). They were centrifugated and storage at -20 °C. The microbial community analysis was carried out with 0.5 g of biomass. The deoxyribonucleic acid (DNA) metagenomic was extracted using commercial kit DNeasy Power Soil (QIAGEN, Hilden, Germany) following the manufacturer's instructions. DNA integrity was evaluated using 1% agarose gel electrophoresis in TAE 1X and quantified on a spectrophotometer (NanoDrop Technologies, Wilmington, DE, USA). 341F and 806R primers [34] with the addition of an "overhang" sequence compatible with the "index" and adapters of the Miseq-Illumina platform were used. The PCR reaction was performed in a final volume of 20 µL, containing 7 µL of 2x Master Mix Prime Time, 4 µL of each primer (1 pmol μL^{-1}) and 5 µL of DNA (1 ng μL^{-1}). Amplification was carried out with initial denaturation at 95 °C for 3 min, followed by 30 cycles at 95 °C for 0.5 min, annealing at 60 °C for 0.5 min, and extension at 72 °C for 0.5 min. The final extension was carried out at 72 °C for 5 min. The amplicons were purified with AMPure XP DNA purification beads (Beckman Coulter, Danvers, MA, USA) according to the manufacturer's instructions. Subsequently, the amplicons were linked to a specific index pair (N7xx and S5xx) for each sample during a second PCR as following: for a final volume of 25 µL, 12.5 µL of 2x KAPA HiFi HotStart ReadyMix, 3 µL of each Nextera XT index, 2.5 µL of the purified product from the first PCR and 4 µL of ultra-pure water. This amplification was carried out with initial denaturation at 95 °C for 3 min., followed by 8 cycles at 95 °C for 0.5 min, annealing at 55 °C for 0.5 min, extension at 72 °C for 0.5 min and final extension at 72 °C for 5 min. Then, the "amplicons" were evaluated regarding the quality and size of the bands using the Bioanalyzer DNA 1000 chip and quantified by real time PCR using the KK4824-Kappa Biosystems kit (Biosciences, Woburn, MA, USA) on Step One Real Time PCR equipment (Applied Biosystems, Foster City, CA, USA). Finally,

these pooled libraries were sequenced on the Illumina MiSeq platform using the V3 kit, 2 × 300 bp paired-end.

The obtained sequences were demultiplexed to split the samples according to the set of the index used. Then, the quality of the sequences was evaluated based on the quality filter of the MiSeq Illumina sequencer, excluding sequences with low-quality values. After this initial screening, the reads were converted to the FASTq format. Then, analyzes following the pipeline developed by the Brazilian Microbiome Project [35] were performed. Taxonomic classification was performed using the core_diversity pipeline of the QIIME package [36]. Sequences within a similarity threshold of 97% were considered operational taxonomic unit (OTU).

2.6 YES assay

2.6.1 Sample preparation

Before the YES assay, samples from the AnOMBR-MD were filtered through a 0.45 µm cellulose nitrate membrane (Unifil - 510.047) and acidified to pH 3 with HCl. The samples were then percolated through C18 cartridges (500 mg / 6 mL, Agilent Technologies) at a flow rate of 10 mL min^{-1} according to the methodology proposed by Do Nascimento et al. [37]. Cartridges were dried under vacuum for 20 min and 4 mL of acetone were used to elute the extracts from the cartridges. The solvent was evaporated and the dried extracts were resuspended in 1 mL of ethanol immediately before use in the YES assay.

2.6.2 Assay procedure

The YES assay was carried out according to the protocols developed by Routledge and Sumpter [16] and Bila et al. [38] with modifications at the Laboratory of Aquatic Ecotoxicology of the Universidade Federal de Viçosa.

Tests were performed in 96-well microtiter plates (Figure 2) and the standard curves were prepared with 12 concentrations ranging from 2,724 ng L^{-1} to 1.33 ng L^{-1}. Ethanol was used as blank solvent control. Ten (10) µL of individual PhAC solution or sample extract was serially diluted in ethanol and tested in duplicate. After evaporation of ethanol from the sample and blank wells, 200 µL of analysis medium (fresh growth medium, 80 mg L^{-1} of CPRG and 4 x 10^7 cells of recombinant yeast) were added to each well. The plates were sealed, shaken for 2 min on a plate shaker and kept at 32 °C. After 72 h incubation, plates were shaken again for 2 min and left to settle for 1 h. Absorbances were then measured at 540 nm for color and 630 nm for turbidity in a Polaris® microplate reader (Celer Biotechnology, Belo Horizonte, Minas

Gerais, Brazil). Two test batches were necessary, with 9 samples from the AnOMBR-MD in each.

Figure 2 - Yes assay microplate after 72 h incubation.

2.6.3 Estrogenic activity calculation

The absorbance of each well was corrected according to Eq. (1):

$$Corrected\ abs = Sample_{540} - (Sample_{630} - Control_{630}) \qquad \text{Eq. (1)}$$

For the E2 standard curve and PhACs, corrected absorbance was plotted versus the concentration and fitted to a four-parameter logistic regression dose-response curve (Eq. (2)), using the package 'dr4pl' [39], in R Program, version 3.2.1 [40].

$$Corrected\ abs = \frac{A_1 - A_2}{1+\left(\frac{x}{EC_{50}}\right)^p} + A_2 \qquad \text{Eq. (2)}$$

where A_1 is the basal induction of estrogenic activity, A_2 is the maximum induction of estrogenic activity, p is the hillslope, EC_{50} is the 50% effective concentration and x is the concentration of the compound.

The estrogenic relative potency (RP) of each PhACs was estimated by Eq. (3) and is defined as the ratio of the standard and the PhACs concentration for the same effect.

$$RP = \frac{EC_{50,E2}}{EC_{50,PhCs}} \qquad \text{Eq. (3)}$$

The estrogenic activity of the samples from the AnOMBR-MD was calculated as E2 equivalents (E2-eq.) by interpolation from the E2 standard curve. Estrogenic activity is calculated by the average of at least 3 wells in which the absorbance has the higher correlation with the dilution. The limit of detection (LOD_{yes}) was defined as the concentration of E2 that

causes an effect equal to the blank's average absorbance plus 3 times its standard deviation. The limit of quantification (LOQ_{yes}) was estimated as the concentration of E2 that causes an effect equal to the blank's average absorbance plus 10 times its standard deviation [41,42].

Total estrogenic activity for the municipal wastewater, with the PhACs in a concentration of 2 µg L^{-1} each, was calculated by the concentration additive model, according to Eq. (4) [43]:

$$E2 - eq_{\cdot mix} = \sum RP_{PhAC} \times C_{PhAC} \quad \text{Eq. (4)}$$

Where $E2\text{-}eq._{mix}$ is the estrogenic activity from the mixture and C_{PhAC} is the concentration of the PhAC.

2.7 Analysis of environmental and human health risk

Environmental and human health risks were evaluated for feed solution and distillate. Hazard quotients (HQ) were calculated for acute and chronic effects as well as for environmental risk, according to Eq. (5):

$$HQ = \frac{MEC}{PNEC} \quad \text{Eq. (5)}$$

where MEC is the measured PhAC concentration or estrogenic activity (E2-eq.) and PNEC is the predicted non-effect concentration. PNEC for acute environmental risk was calculated by dividing the half-maximal effective or lethal concentration (EC50 or LC50) by an assessment factor of 1000, according to the European Commission [44] (Supplementary material, Table S1). For chronic environmental risk, the no observed effect concentration (NOEC) was divided by the assessment factor, according to Table S1, depending on the available data.

Human health risk (HQ_h) was estimated by Eq. (6), where DWGL is the drinking water guideline level, calculated by Eq. (7).

$$HQ_h = \frac{MEC}{DWGL} \quad \text{Eq. (6)}$$

$$DWGL = \frac{TDI \times BW \times f}{DI} \quad \text{Eq. (7)}$$

where TDI is the tolerable daily intake for each PhAC or E2 equivalent, in the case of estrogenic activity, BW is the body weight, considered 70 kg, f is the relative contribution of water exposure, considered equal to 100% in the case of PhACs, and DI is the daily input of water (2 L d^{-1}) [45].

For both environmental and human risk assessment, the hazard index (HI) was also calculated to assess the cumulative risk in AnOMBR-MD distillate by the concentration addition model [46]. HI was calculated as the sum of the individual HQs for all seven PhACs (Eq. (8)).

$$HI = \sum_{i=1}^{n} HQ_i \qquad \text{Eq. (8)}$$

HQ and HI values were classified as high risk (HQ or HI > 1), medium risk (0.1 ≤ HQ (HI) ≤ 1), low risk (0.01 ≤ HQ (HI) < 0.1) and negligible risk (HQ (HI) < 0.01) [27,33]. Values of L(E)50, NOEC, and DWGL were taken from literature and are presented in the supplementary material (Tables S2 – S4).

The incremental lifetime carcinogenic risk (ILCR) was estimated by the model proposed by US EPA [47] (Eq. (9)).

$$ILCR = \frac{MEC \times DI \times EF \times ED \times CSF}{BW \times AT} \qquad \text{Eq. (9)}$$

where EF is the exposure frequency (considered equal to 365 d per year), ED is the exposure duration (70 years), AT is the average time (equal to 25,550 d), and CSF is the cancer slope factor (linear low-dose cancer potency factor) for the PhACs kg d mg^{-1}. The CSF depends on the compound; however, no information was found for the PhACs used in this study. On the other hand, CSF for 17β-estradiol is equal to 39 kg d mg^{-1} [48], and ILCR was estimated using the estrogenic activity as MEC. According to US EPA [47], when ILCR > 10^{-4}, the risk is considered unacceptable, for 10^{-4} < ILCR < 10^{-6}, the risk is acceptable, and risk is negligible when ILCR < 10^{-6}.

Environmental and human health risks were estimated for the average PhAC concentrations found in the AnOMBR-MD distillate. Detection limits were used in risk calculations for compounds that were not detected, according to the precautionary principle [49].

3 Results and discussion

3.1 Organic matter and nutrients removal

Mixed liquor (ML) pH remained relatively constant at about 8.2 and the same was observed for DS and distillate (Table 3), with a pH of 7.9 and 8.2, respectively. The low pH variation can be explained by the high ML alkalinity and methanogenic *Archaea* activity that

counteracted the pH-reducing effects of volatile fatty acids (VFA). VFA concentrations lower than reported by other authors in AnOMBR is evidence of high methanogenic activity, which produces biogas that could be recovered [15]. VFA and DOC concentrations in DS and distillate were much lower than in ML, with DOC removals of 96.2% by FO and 97.2% overall in the AnOMBR-MD observed. Furthermore, DOC in ML ranged from 48.1 to 58.3 mg L^{-1}, suggesting that biodegradation played an important role, being responsible for more than 70% of the removal, even with salinity build-up, since higher DOC in the bioreactor was expected, of almost 600 mg L^{-1}, considering the continuous entering of organic matter from the feed solution.

Nutrient accumulation in the bioreactor was expected due to anaerobic treatment, in which organic nitrogen is converted to its inorganic form. N-NH_4^+ in the DS reached almost 50 mg L^{-1} after 15 days of operation, caused by its passage through the FO membrane to the DS. FO ammonia rejection was 88.9%, and DS presented an average N-NH_4^+ concentration of 22.9 mg L^{-1}, within the range previously reported for AnOMBR, of 10 to almost 40 mg L^{-1} [50]. A significant N-NH_4^+ concentration was detected in the distillate since ammonia is volatile and can pass through the MD membrane. Ammonia transport could be reduced with pH adjustment in the DS to below 6 [51].

The maximum P-PO_4^{3-} concentration in the ML was 31 mg L^{-1}, and the overall removal was around 98.0%, with concentrations in distillate below the method detection limit (0.3 mg L^{-1}). Several studies have been carried out to recover phosphorus in OMBRs [23,52]. Indeed, the FO membrane presented about 98% rejection of P-PO_4^{3-} and the feasibility of recovering this nutrient and nitrogen in the AnOMBR-MD should be evaluated.

Table 3 - Average contaminant concentration and removal efficiency in AnOMBR-MD operation

Parameter	ML	DS	Distillate	R_{FO} (%)	$R_{AnOMBR+MD}$ (%)
pH	8.2 ± 0.2	7.9 ± 0.3	8.2 ± 0.5	-	-
Alkalinity ($mgCaCO_3\ L^{-1}$)	696 ± 114.7	230 ± 211.6	66.3 ± 23.2	-	-
VFA ($mgHAc\ L^{-1}$)	47.2 ± 25.9	14.8 ± 10.2	0.4 ± 1.1	-	-
DOC ($mg\ L^{-1}$)	57.8 ± 18.1	2.2 ± 2.0	2.1 ± 2.1	96.2	97.2
$N\text{-}NH_4^+$ ($mg\ L^{-1}$)	37.8 ± 6.9	22.9 ± 10.4	7.9 ± 3.2	88.9	77.8
$P\text{-}PO_4^{3-}$ ($mg\ L^{-1}$)	20.9 ± 9.8	0.8 ± 1.2	0.3 ± 0	98.3	98.0

3.2 AnOMBR-MD permeate flux and reverse salt flux

Permeate flux in FO was about 3.33 kg m^{-2} h^{-1} at the beginning of AnOMBR-MD operation, and after 30 days, J_{FO} stabilized at 0.71 kg m^{-2} h^{-1}, 20% of its initial value (Figure 3a). At the beginning of the operation, since J_{FO} was higher than J_{MD}, a dilution in DS salt concentration was verified, reducing the osmotic pressure difference across the FO membrane. FO membrane fouling may have contributed to the flux decline. Another reason for the decline in J_{FO} was salinity build-up in the bioreactor that lowered the FO driving force (Figure 3b). Ion accumulation is influenced by the reverse salt flux (J_s) and the dissolved compounds entering the bioreactor [26]. The latter is more challenging to control since the FO membrane has a high rejection for dissolved compounds, while the former can be reduced, depending on salt diffusivity. After 50 days of operation, the conductivity in the ML stabilized around 60 mS cm^{-1} (Figure 3b), which led to an increase in the osmotic pressure in the bioreactor to 30 bar. Thus, the osmotic pressure difference across the FO membrane was reduced to less than 80 bar, meaning that a better solute than NaCl for the DS is needed, as already demonstrated in previous studies [53,54]. Furthermore, elevated ion concentration in the bulk sludge can cause osmotic stress for the bioreactor microorganisms, reducing their biological activity and, therefore, the overall performance in the AnOMBR-MD [26,53].

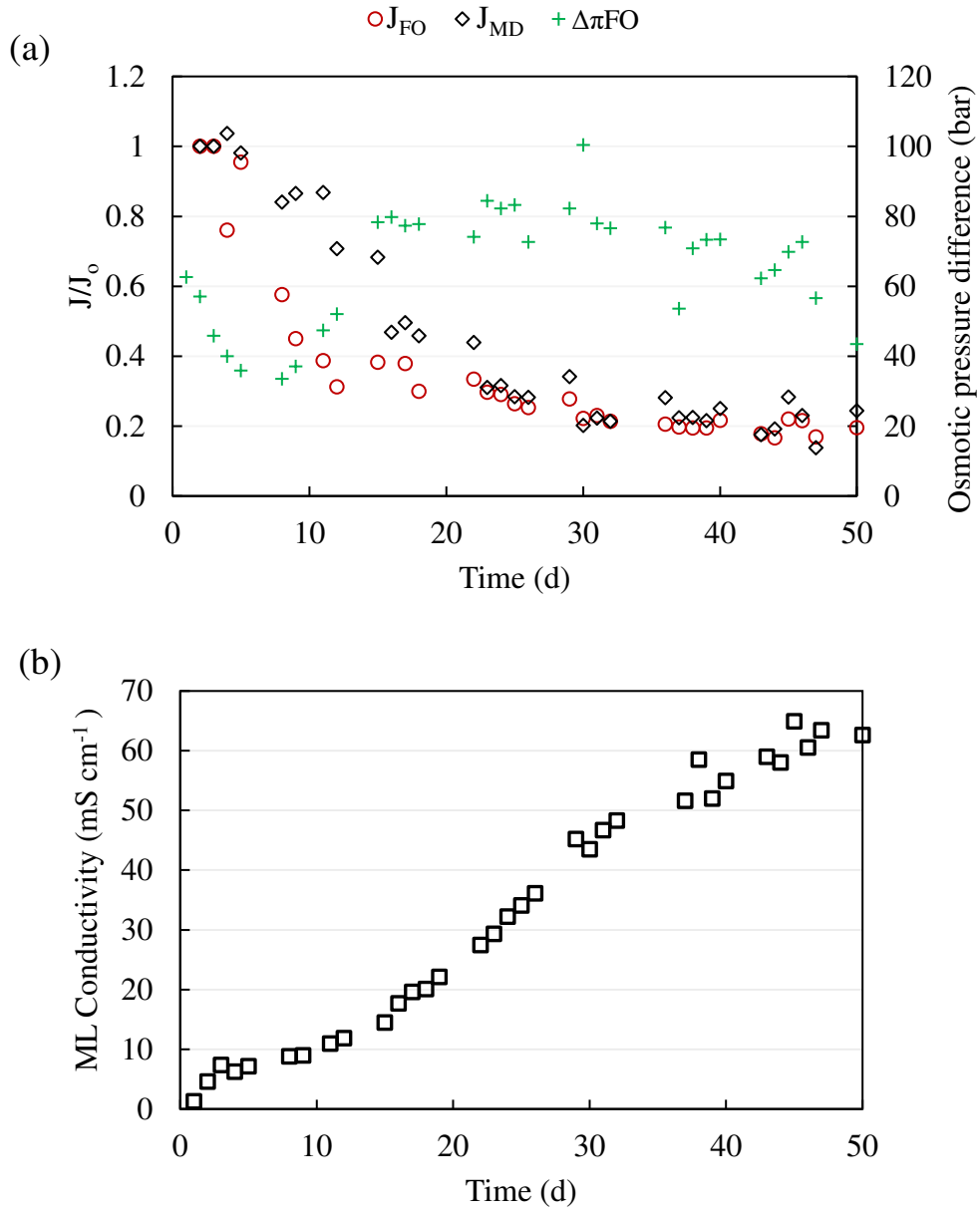

Figure 3 - (a) Normalized permeate flux in FO and MD membranes and osmotic pressure difference in FO and (b) ML conductivity during AnOMBR-MD operation.

A less sharp reduction in J_{MD} was observed since MD did not depend on the salinity of the feed solution, which was DS. The initial J_{MD} was 2.35 kg m^{-2} h^{-1} and it stabilized at 0.81 kg m^{-2} h^{-1}, close to the J_{FO}, after 50 days. Unlike FO, fouling had less impact on MD performance than concentration and temperature polarization. When water vapor permeates the MD membrane, NaCl accumulates at the feed membrane surface, which can lead to pore blocking and flux decline [55]. The bulk temperature in MD was 25.5 ± 2.2 °C. However, with temperature polarization, described as the reduction in the temperature difference across the membrane, the vapor pressure difference - the MD driving force - was reduced [25].

Nevertheless, MD salt rejection was greater than 99.5%, making it suitable for DS reconcentration and water recovery processes in an AnOMBR treating municipal sewage.

3.3 Microbial community diversity in the bulk sludge

The presence of PhACs could inhibit the proliferation of microorganisms. On the contrary, various authors have reported an increase in bacterial diversity, after the addition of PhACs [56–58]. Indeed, the microbial community richness and diversity presented a significant increase in the AnOMBR-MD, supported by the Chao 1, Shannon and Coverage estimators in Table 4. These findings were not expected, since the sludge retention time was 45 d, really close to the operation time. A great change in bacteria phylum level was observed (Figure 4). The sludge used as inoculum was composed mainly by Synergistetes (83.4%) and Caldiserica (5.4%). Meanwhile, the dominant microorganisms after 50 days operation were Proteobacteria (34.9%), Synergistetes (30.3%), Planctomycetes (11.7%) and Caldiserica (5.8%), followed by Bacteroidetes, Chloroflexi, Actinobacteria, Firmicutes, TM7, [Thermi], WS6, NKB19 and Thermotogae. Chen et al. [59] found that Firmicutes abundance must be higher than Bacteroidetes for the anaerobic system to have better performance. In the seed sludge, the relation between Firmicutes and Bacteroidetes was 1.47, but it reduced to 0.34 after 50 days, which could induce system instability and a loss of overall removal efficiency. Compared to the studies of Muñoz Sierra et al. [60] and Wang et al. [61], under anaerobic, mesophilic, and saline environments, only the phyla TM7, [Thermi] and NKB19 were not identified in their research. However, different from the present study, Proteobacteria abundance reduced in those conditions.

In an AnOMBR with a complete rejection of MLVSS, a long sludge and micropollutants retention time is achieved allowing not only the increase in biodegradation of recalcitrant compounds but also the suppression of less salinity tolerant microorganisms. Additionally, the increment in richness and diversity, may have permitted the degradation of different compounds in the AnOMBR-MD, because of the great number of functions in the microbial community. Nevertheless, an investigation in a long-term operation should be conducted in this kind of MBR in future studies.

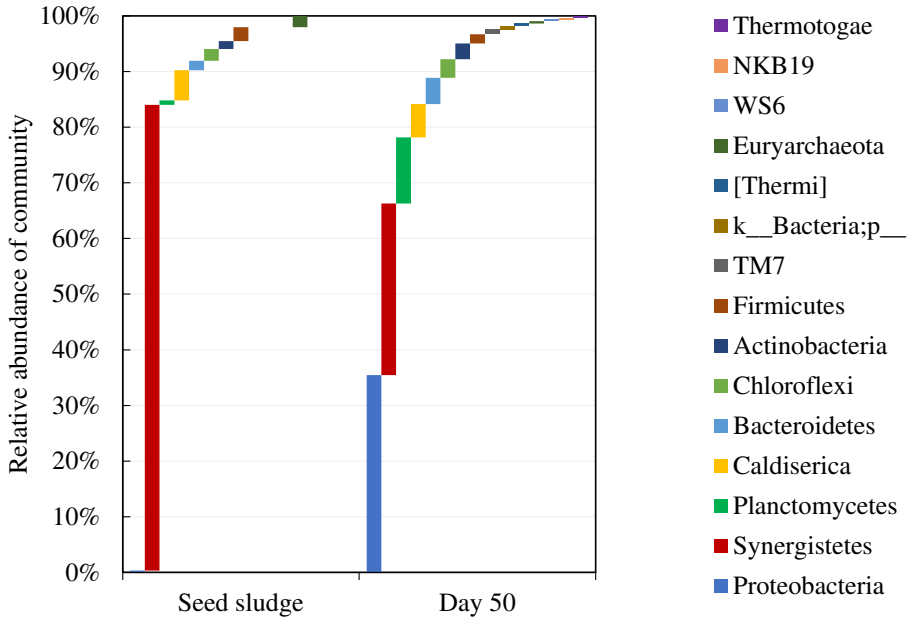

Figure 4 - Microbial community abundance of the phylum in bulk sludge of the AnOMBR-MD.

Table 4 - Richness and diversity estimators of the community

Sample	OTU[a]	Chao 1	Shannon	Coverage
Seed sludge	137	155.9	6.34	0.99589
Day 50	874	971.5	7.61	0.97197

[a]OTU: operational taxonomic units.

Microbial community dynamics for the genus level of both bacteria and archaea are presented in Figure 5. For bacteria (Figure 5a), TTA_B6 was the most abundant genus and reduced significantly during the AnOMBR-MD operation. This uncultivated organism seems to be related to full-scale anaerobic bioreactors, decreasing its abundance under lab-scale conditions [62]. Unclassified organisms from Xanthomonadaceae were the second most abundant genus at day 50 and it was not found in the inoculum. Despite being considered obligate aerobe organisms, Hao et al. [63] found out that Xanthomonadaceae was one of the most abundant families in anaerobic sludges digesters, suggesting that this organism could use some electron acceptors other than oxygen, like nitrate and sulfate. *Planctomyces* and *unclassified Pirellulaceae*, which belong to Planctomycetes phylum, have species adapted to both aerobic and anaerobic conditions [64]. Furthermore, *Planctomyces* includes the specie *Planctomyces brasilien*sis, found in hypersaline ponds [65], and thus, had better performance over other species.

Concerning methanogenic archaea (Figure 3b), its relative abundance on the microbial community decreased from 1.30% to 0.38%, despite the increment in OTUs after 50 days (from 20 to 133). Thus, an impact on methane production is expected, reducing the possible resource recovery from the AnOMBR-MD system. Methanogenic archaea are extremely sensitive to salinity, micropollutants, VFA, and ammonia [26,63]. Compared to the beginning of the operation, ammonia concentration decreased, while VFA increased slightly from 6.2 to 34.6 mgHAc L^{-1} (Table S5). However, as discussed in section 3.1, pH remained relatively constant due to the high alkalinity. PhACs accumulation could also impact microbial community change, but as shown by Symsaris et al. [66], higher biomass concentration may reduce the effect of micropollutants on methanogenic communities. Therefore, the parameter with more influence on methanogenic organisms is salinity build-up, which could be mitigated using a draw solute with lower diffusivity [67]. Reduction in salinity in the bioreactor could result in better biodegradation of recalcitrant compounds, as PhACs, and reduce their concentration in the mixed liquor and their impact on the microorganisms. *Methanobacterium* was the only genus representing Methanobacteria class, and Methanomicrobia was assigned to *Methanomicrobiales, Methanosaeta,* and *Methanolinea*. *Methanosaeta* was the only acetoclastic methanogen present in the samples and doubled its abundance in the bulk sludge, from 5.0% to 10.5%, even though it is more vulnerable to salinity than *Methanosarcina* [63]. Nevertheless, *Methanosaeta* is more abundant in mesophilic conditions, around 37 °C [68]. *Unclassified Methanomicrobiales* were not detected in the inoculum and were the most abundant group on day 50 (67.7%), indicating that they are less affected by salinity and temperature than *Methanolinea* and *Methanobacterium,* whose relative abundance was reduced in the community. Therefore, *Methanomicrobiales* has an important role in methanogenesis, and hydrogenotrophic may be the dominant pathway in methane production in AnOMBR.

On the other hand, sulfate-reducing bacteria (SRB), not found in the inoculum, increased its abundance to 0.42%, represented by the genera *Desulfovibrio* and *Desulfomicrobium*, and unclassified families Desulfobacteraceae, Desulfovibrionaceae, and Thermodesulfobiaceae.

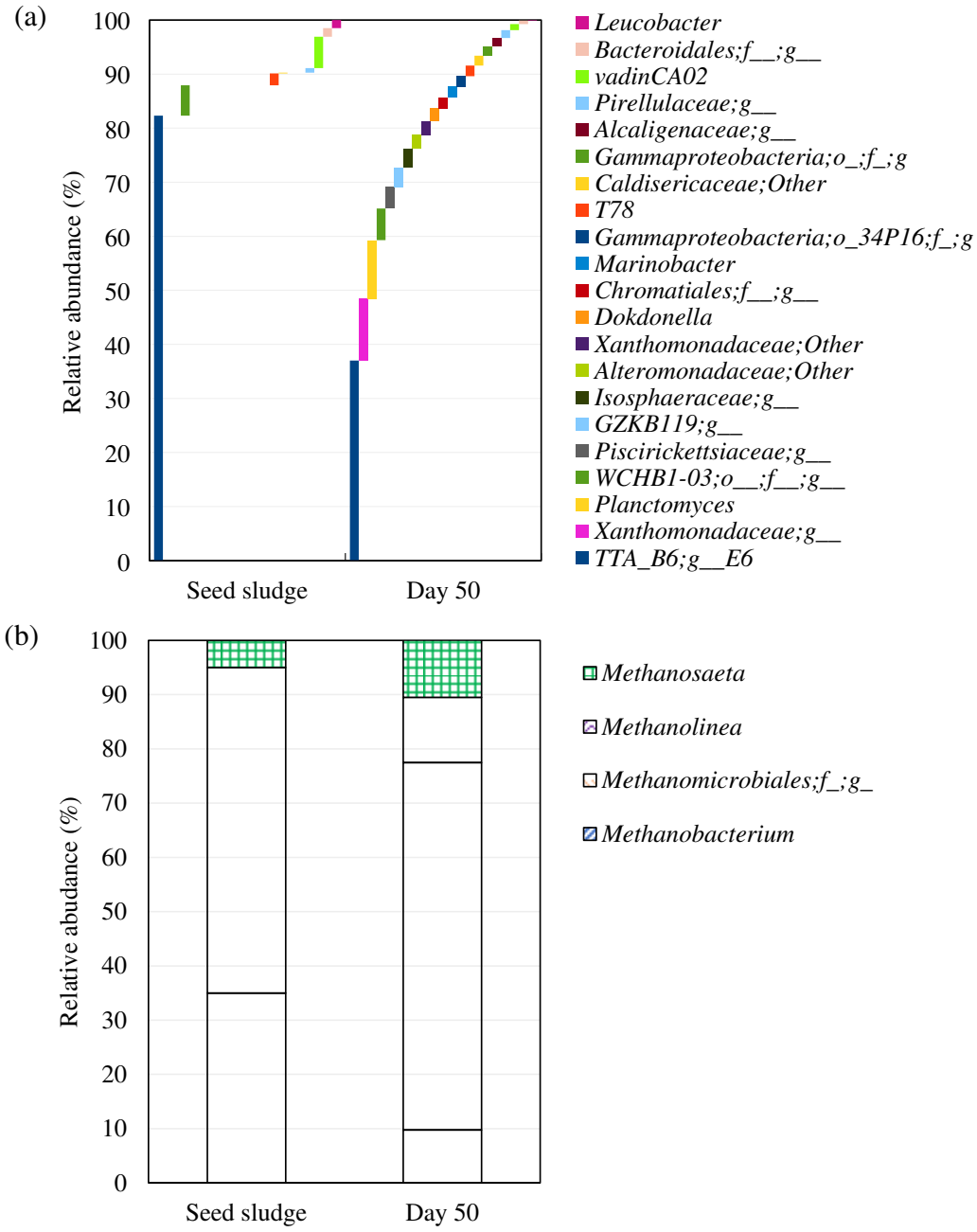

Figure 5 - Microbial community composition in bulk sludge of the AnOMBR-MD. (a) Abundance of the major bacterial genera (> 1%); and (b) abundance of the archaea genera. (f_ and g_ mean that it was not possible to classify the family and the genus, respectively).

3.4 Estrogenic activity of the selected PhACs

EC_{50} values for the 17β-estradiol standard and the 7 PhACs in the YES assay are listed in Table 4. 17α-ethinylestradiol presented relative potency (RP) close to 1, indicating that it had the same activity as 17β-estradiol. RP values reported in the literature varied from 0.67 to 1.07.

Besides 17α-ethinylestradiol, only fluconazole had estrogenic activity, but only at a concentration of 6.04 mg L^{-1}, with RP of almost 10^{-5}, signifying that it is a weak estrogenic compound. The other 5 PhACs did not present any effect over the range of concentrations tested. Fent et al. [69] and Isidori et al. [70] reported fenofibrate and prednisone exhibited estrogenic activity at concentrations 7 to 8 order of magnitude higher than 17β-estradiol, which are not found in the environment and were therefore not tested in this study. No estrogenic activity was detected for ketoprofen. Wieczerzak et al. [13] demonstrated that this PhAC had antiestrogenic activity, which is also considered a disrupting effect and in the presence of estrogenic compounds may reduce their biological activity. Betamethasone and loratadine did not exhibit any activity even at the highest concentrations tested, and no information on their possible estrogenicity was found in the literature.

Therefore, it is important to have an effective treatment capable of removing the 7 PhACs, which have been found in wastewater, surface, and drinking water [27,28] and may present estrogenic or antiestrogenic effects in aquatic organisms and human beings.

Table 5 - EC_{50} and RP for the selected PhACs in YES assay

PhACs	**Concentration range (ng L^{-1})**	**EC_{50} (ng L^{-1})**	**RP[a]**	**Reference**
17β-estradiol	1.33 to 2.72 x 10^3	59.67	1	This study
17α-ethinylestradiol	1.17 to 2.40 x 10^3	57.93	1.03	This study
			1.07	[57]
			0.88	[58]
			0.81	[59]
			0.71	[60]
			0.69	[61]
			0.67	[5]
Betamethasone	2.44 to 11.0 x 10^6	ND[b]	-	This study
Ketoprofen	2.44 to 16.5 x 10^6	ND	-	This study
Fenofibrate	2.44 to 10.5 x 10^6	ND	-	This study
			2.94 x 10^{-7}	[55]
			1.48 x 10^{-7}	[54]
Fluconazole	2.44 to 11.0 x 10^6	6.04 x 10^6	9.88 x 10^{-6}	This study
Loratadine	2.44 to 10.0 x 10^6	ND	-	This study
Prednisone	2.44 to 9.50 x 10^6	ND	-	This study
			3.57 x 10^{-8}	[55]

[a]Calculated with the concentrations in ng L^{-1}; [b]ND: Not detected (LOD = 15.98 ng L^{-1} E2-eq.).

3.5 AnOMBR-MD estrogenic activity removal

Municipal sewage's estrogenic activity before the addition of PhACs was equal to 9.2 ng L^{-1} E2-eq., a value within the range reported in the literature [71–73]. Sewage's estrogenicity was likely caused by hormones, e.g., 17β-estradiol, 17α-ethinylestradiol, and estrone, but also by phenolic compounds, such as nonylphenol and bisphenol A, as well as phthalates, like dibutyl phthalate, that are frequently detected in municipal sewage [4]. After adding the 7 PhACs to the sewage used as feed solution to the AnOMBR-MD, estrogenicity increased 335%, reaching a value of 6,921 ng L^{-1} E2-eq. This indicates that the mixture of PhACs and wastewater had a synergistic interaction: the effects of some compounds were increased in others' presence since the $E2\text{-}eq._{mix}$ calculated by the concentration additive model was only 2,069 ng L^{-1} E2-eq. Therefore, PhAC concentration alone is not sufficient to evaluate the potential risks of complex mixtures. The use of *in vitro* assays to assess these risks added great value to the investigation of the micropollutants.

The concentration of estrogenic compounds in the AnOMBR-MD mixed liquor (Figure 6a) after 12 days of operation was 4 times lower than in the feed solution, suggesting that anaerobic treatment was capable of removing these compounds. From day 23 on, a greater reduction in mixed liquor estrogenic activity was observed, with values of 173 ng L^{-1} E2-eq., corroborating the removal by biological treatment. Indeed, the biological removal of estrogenic activity varied from 75 to 97% (Figure 6b) over time. Even with the observed change in the microbial community and the expected instability of the system, after 50 days, biodegradation of estrogens was not affected, proving the advantage of AnOMBR-MD for the treatment of municipal sewage.

Various studies demonstrated that anaerobic treatment had low or no removal of EDCs [73–75]. The 3 main mechanisms for estrogenic compounds removal are: biological processes, either by metabolic or co-metabolic biodegradation; adsorption to the sludge; and volatilization [76]. In anaerobic treatment, as there is no aeration and because of the low Henry's constant values (Table S1), volatilization certainly play a negligible role. Therefore, it is expected that sorption and biodegradation are the dominant processes. According to Prasse et al. [77], biological removal of organic compounds occurs by the oxidation of alcohols and aldehydes to carboxylic acids, N-dealkylation, ester cleavage and hydroxylation. Although this biotransformation is not sufficient to remove estrogenic recalcitrant compounds, the longer retention time of the PhACs and EDCs in the AnOMBR-MD, combined with the increment in microbial richness and diversity permitted relatively high removal efficiencies, minimizing the

effect of salinity build-up in the bioreactor. Additionally, the increased temperature in the bioreactor (37.7 ± 3.3 °C), due to recirculation of DS at 45 °C, may have had a positive impact on estrogenicity removal, by increasing microbial activity [78].

Estrogenicity was detected in DS on day 12, but it was below the LOQ (4.9 ng L^{-1} E2-eq.), indicating high rejection of EDCs by the FO membrane (Figure 6b). No estrogenic activity was detected in DS, and FO membrane rejection was greater than 98.6% for the other monitoring days. No estrogenic effect was detected (LOD < 2.3 E2- eq. ng L^{-1}) in the distillate samples, and the overall efficiency of the AnOMBR-MD was greater than 99.97%.

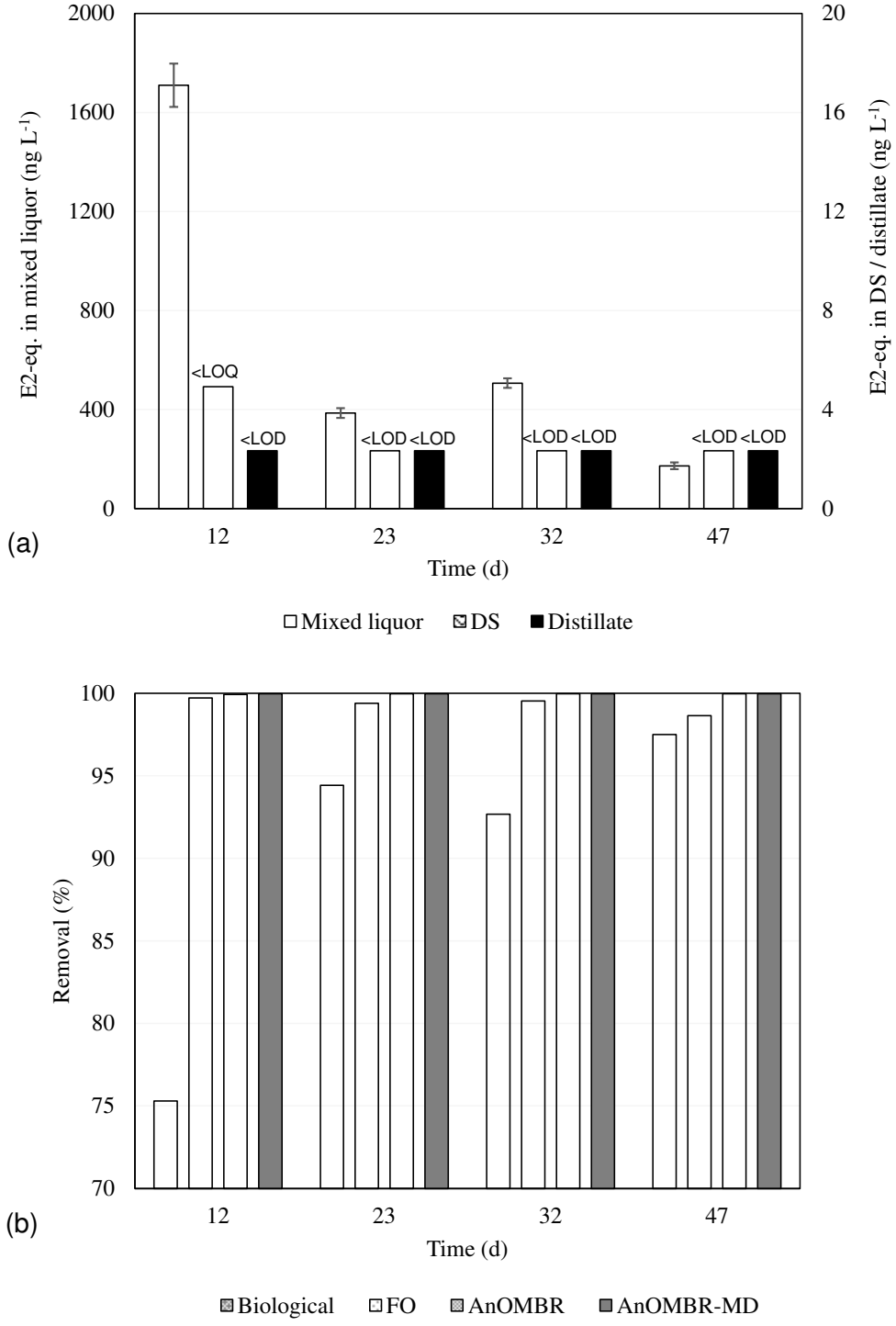

Figure 6 - (a) Estrogenic activity in the mixed liquor, DS and distillate; (b) Estrogenic activity removal efficiency in the AnOMBR-MD. LOQ and LOD are mean limits of quantification and limit of detection, respectively. Error bars for DS and distillate, as well as for removal efficiency were not calculated, because, in all samples, estrogenic activity was bellow LOQ or LOD.

3.6 AnOMBR-MD PhACs removal

The removal of the selected PhACs in the AnOMBR-MD is presented in Table 5. Anaerobic biological treatment with FO (AnOMBR) effectively removed fenofibrate and loratadine since they were not detected in DS at all. The high AnOMBR efficiency was likely due to size exclusion and biodegradation. As already shown by Ricci et al. [24], the FO CTA membrane promotes better rejection of compounds with molar weights > 270 g $mol^{-1,}$ and the selected PhACs, except ketoprofen, have molar masses higher than 358 g moL^{-1}. For ketoprofen, with the lowest molar mass (254.3 g moL^{-1}), a concentration of 3 µg L^{-1} was found in DS. Regarding fluconazole, the most hydrophilic of the PhACs (log K_{OW} = 0.56), the interaction with the CTA membrane may have facilitated its passage to the DS. Faria et al. [33] observed that 17α-ethinylestradiol and betamethasone were predominantly removed by biotic mechanisms (73.10% and 94.88%) compared to abiotic mechanisms (8.08% and 0%) under anaerobic conditions. For prednisone, loratadine, and fenofibrate, the authors recognized that removal was mainly due to abiotic factors like sorption and chemical degradation.

The concentration of 17α-ethinylestradiol was not expected to increase in DS, given its high hydrophobicity (log K_{ow} = 3.9). However, biodegradation rates decreased with salinity build-up in the bioreactor, leading to 17α-ethinylestradiol accumulation and higher concentrations in DS, despite the high FO membrane rejection (> 95.88%). However, estrogenicity associated with this level of 17α-ethinylestradiol was not detected in DS (Figure 6a). It may be explained by an effect of the DS matrix, or, more likely, by an antagonistic interaction of the compounds present in DS, such as ketoprofen, reported to be an antiestrogenic EDC [13].

Only betamethasone, fluconazole, and prednisone reached the distillate (Table 5). Although the prednisone concentration in DS was below the detection limit, it was detected in the distillate, which suggests that DS salinity may have caused ion suppression and decreased the sensibility for the analytes (Table 1) [79]. Nevertheless, in distillate concentrations, PhACs concentrations were lower than 157 ng $L^{-1,}$ and the AnOMBR-MD removed more than 97.41% of prednisone and 99.98% of loratadine. Therefore, anaerobic treatment coupled with FO and MD may have synergistic effects and enhance municipal sewage treatment containing micropollutants.

Table 6 - PhACs concentration in the DS and the distillate and removal efficiency in the AnOMBR-MD

PhACs	C_{DS} (ng L^{-1})	C_{dist} (ng L^{-1})	R_{AnOMBR} (%)	$R_{AnOMBR-MD}$ (%)
17α-Ethynilestradiol	9008.55 ± 2922	< 83.61	90.54 ± 7.4	> 97.88
Betamethasone	124.39 ± 136	96.28 ± 86	94.41± 0.47	98.22 ± 3.20
Fenofibrate	< 102.83	< 1.09	> 99.79	> 99.94
Fluconazole	3561.84± 909	90.13 ± 10	92.67 ± 4.55	98.29 ± 0.20
Ketoprofen	3070.40± 639	< 0.81	97.57 ± 2.10	> 99.97
Loratadine	< 20.08	< 0.71	> 99.44	> 99.98
Prednisone	< 59.55	74.33 ± 41	> 97.02	97.41 ± 1.40

Hence, bioanalytical tools combined with detection and identification of micropollutants are fundamental for evaluating the treatment of wastewater containing PhACs and EDCs. Also, toxicity tests, which are required by most legislation, may also corroborated to a better assessment of treatment performance.

3.7 Environmental and human health risk assessment

Both acute and chronic environmental risks in the distillate were classified as low or negligible for all PhACs (Figure 7), suggesting they do not present a risk to aquatic organisms when assessed individually. On the other hand, the acute cumulative risk (HI) of the PhACs was characterized as medium, evidence that the mixture of compounds in distillate can increase environmental risk. This result raises concern about biologically active compounds in the environment since more than 600 have been detected in environmental matrices [2,46]. Considering that PhACs will not be found alone in these matrices, it is necessary to evaluate the cumulative risk of PhACs to better represent their potential environmental impact.

Environmental risks were also assessed considering the estrogenic activity in E2-eq. (Figure 7). The acute risk was classified as medium, while the chronic risk was high. The estrogenic activity risks were higher than the cumulative risk, HI, indicating that the concentration addition model did not consider compound interactions and may have underestimated the risk. Therefore, the use of bioassays together with a suitable model to calculate the effect of the mixture of compounds are necessary to avoid underestimating risk of environmental samples.

It has been reported that just 1 ng L^{-1} E2-eq. can cause disturbances in aquatic organisms [44], making it important to detect estrogenic activity and assess ecological risks, even for compounds present at very low concentrations. In this study, due to the volume of distillate used in solid-phase extraction, the detection limit for estrogenic activity, 2.34 ng L^{-1} E2-eq.,

was relatively high. It limited the possibility to evaluate extremely low concentrations of E2-eq., and possibly artificially inflated the acute and chronic environmental risks by considering the LOD as the detected value in the calculation.

Acute and chronic environmental risks reduction was notable (Figure 7). The municipal sewage spiked with PhACs (feed solution) presented high or medium risks, that were reduced to low or negligible after treatment, explained by the high AnOMBR-MD efficiency in removing PhACs and estrogenic activity. Faria et al. [33] evaluated the removal of these seven PhACs by an anaerobic expanded granular sludge bed (EGSB) reactor combined with ultrafiltration (UF) and the permeate presented medium acute risk for ketoprofen. In the present study, the permeate presented both low acute and chronic risk for all the PhACs, demonstrating the better performance of the AnOMBR-MD. Other authors assessed the risks related to PhACs in WWTPs. Muriuki et al. [80] evaluated the environmental risks related to eight PhACs in a wastewater treatment by stabilization ponds. The study showed that the risk was considered moderate or high for seven of the compounds detected in the effluent. Ramírez-Morales et al. [81] assessed the environmental risk of PhACs in 11 WWTPs, mostly using activated sludge system with extended aeration. Out of the 33 PhACs evaluated in the treatment plants' effluent, 46.9% presented a high risk, and 18.8% exhibited medium risk. This reinforces the efficiency of the AnOMBR-MD in removing environmental risks, when compared to other treatment systems.

The PhACs evaluated individually presented negligible human health risk (Figure 8), except for 17α-ethinylestradiol, which presented a high risk due to the high LC-MS method detection limit. This was confirmed by the treatment's efficiency in removing estrogenic compounds, as discussed in section 3.4. The mixture of PhACs was also classified as a high human health risk due to 17α-ethinylestradiol. In the study of Faria et al. [33], only 17α-ethinylestradiol presented a high risk for EGSB effluent, for the same reason as in the present study. This illustrates the importance of carrying out estrogenic activity assays together with the detection and quantification of pharmaceuticals so that the effects caused by micropollutants are more accurately estimated, even at lower concentrations. Anyway, studies show that the risk to human health related to drugs in drinking water is low or negligible, even in conventional water treatment systems [28,82,83]. However, the potential of PhACs to cause long-term effects cannot be neglected [3].

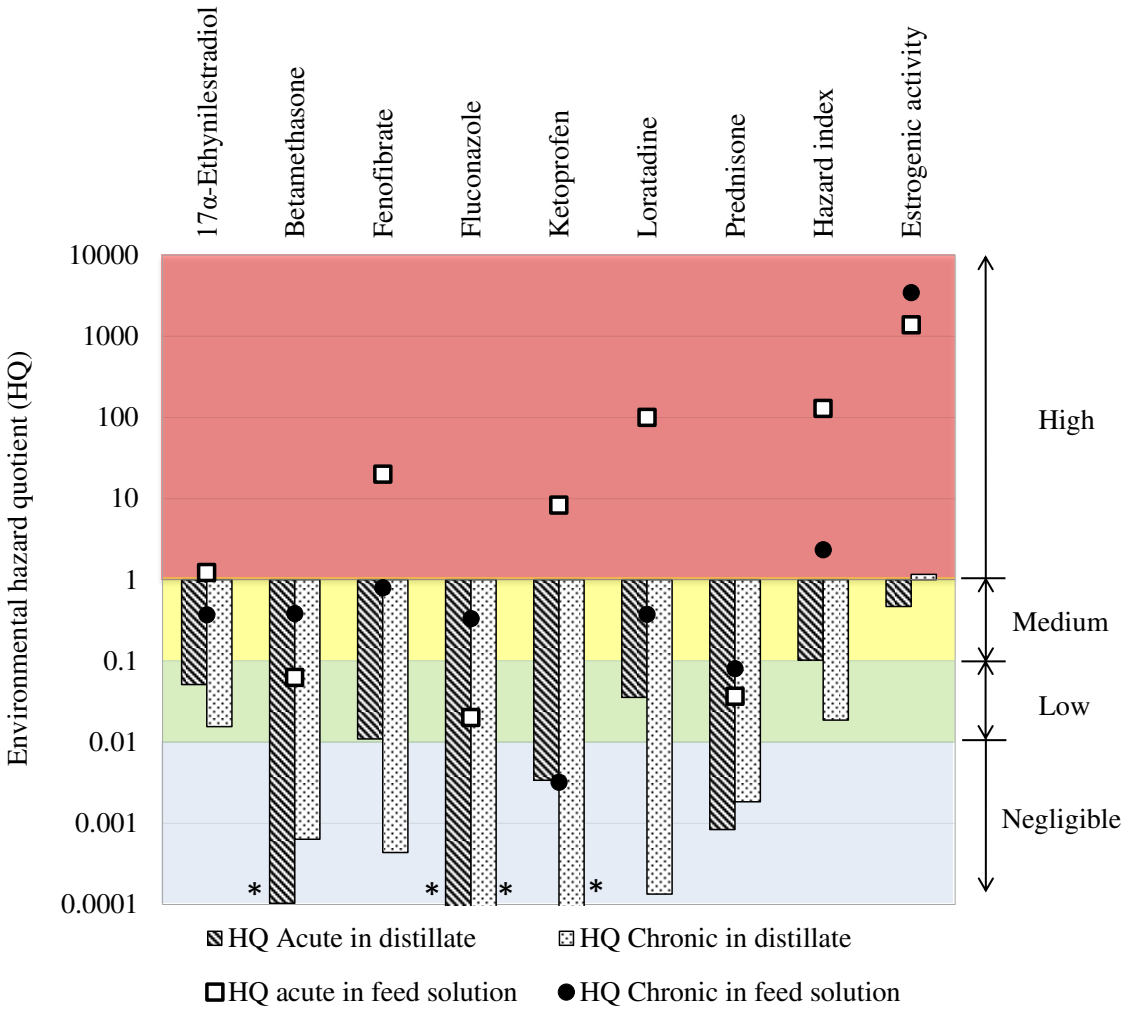

Figure 7 - Environmental risk assessment for distillate. * means HQ values are below 0.0001. Hazard index is the sum of HQ for the PhACs.

The estrogenic human health risk was classified as medium, but some authors would consider it insignificant since the HQh value was less than 1 [14,49]. The human health risk in FS was considered high for most of the compounds evaluated, which is a potential problem since many water and wastewater treatment plants cannot remove PhACs [28,29]. It is important to note that the risks were reduced considerably in the distillate, which exemplifies the efficiency of AnOMBR-MD.

The cancer risk was also measured, considering the estrogenic activity in the distillate. The estimated ILCR value was 2.6×10^{-6}, which is considered an acceptable value for drinking water, according to the US EPA classification [47].

Even though risk assessments for estrone and other EDCs were not carried out in this study, it was demonstrated that the treatment of municipal sewage by the AnOMBR-MD could

effectively reduce the human health risk related to EDCs by evaluating estrogenic activity with YES assay.

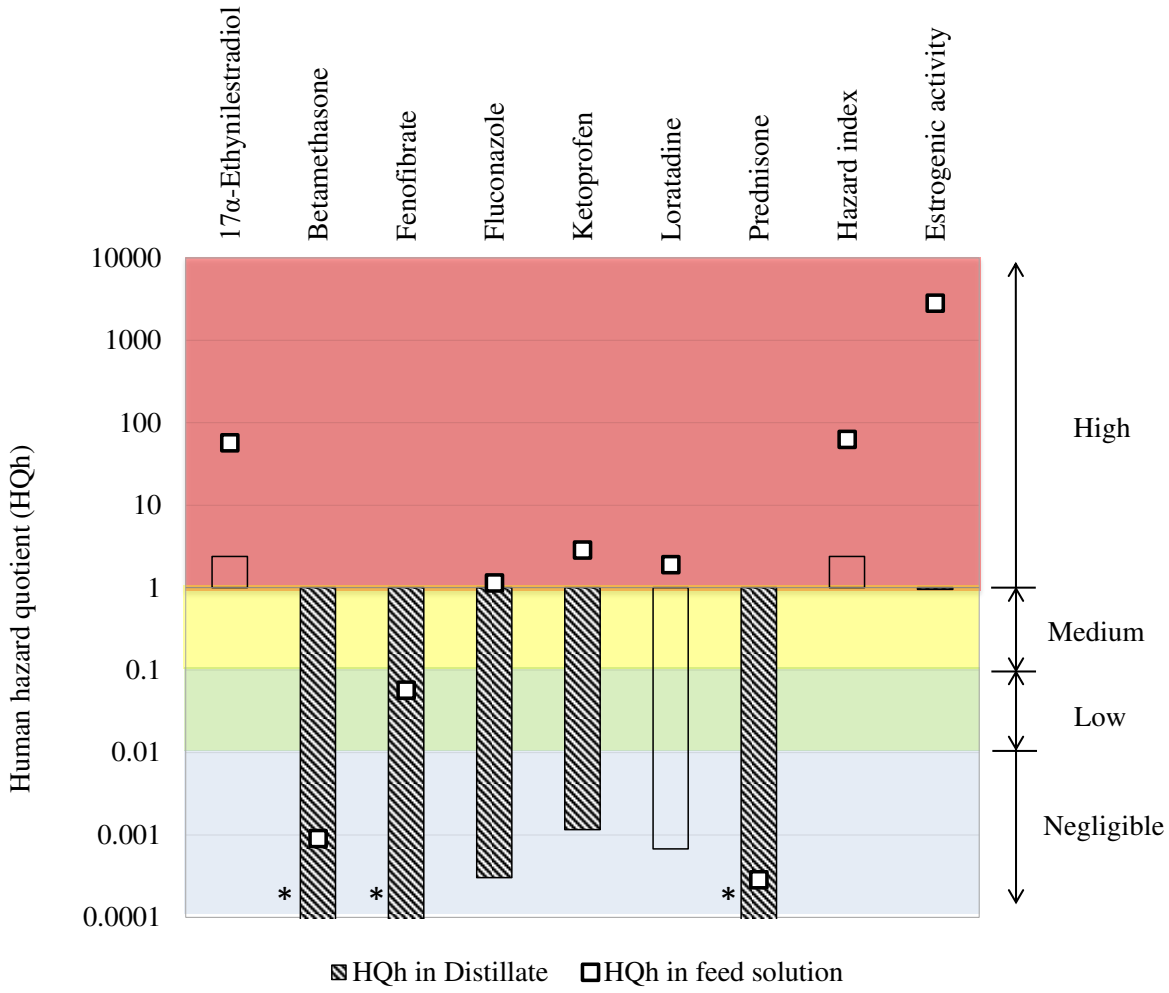

Figure 8 - Human health risk assessment for distillate samples. * means HQh values are below 0.0001. Hazard index is the sum of HQh for the PhACs.

4 Conclusions

The AnOMBR-MD successfully treated municipal sewage containing PhACs and estrogenic activity. Despite the low permeate fluxes of 0.71 kg m^{-2} h^{-1} in FO and 0.81 kg m^{-2} h^{-1} in MD, and the change in the microbial community, the overall removal efficiency of DOC, P-PO_4^{3-}, N-NH_4^+, PhACs, and estrogenic activity reached 97.2, 98.0, 77.8, >96.4 and >99.97%, respectively. Among the PhACs, only 17α-ethinylestradiol and fluconazole had estrogenic activity for the concentrations tested in the YES assay.

Environmental risk assessment related to PhACs in distillate showed that the treatment greatly reduced the HQ and HI values. Nevertheless, the chronic environmental risk based on estrogenic activity was classified as high because of the relatively high detection limit in the YES assay. The high detection limit of LC-MS for 17α-ethinylestradiol and the fact that this value has been considered in the risk assessment has highly contributed to the identified high potential human health risk. Nevertheless, since the human health risk caused by estrogenic compounds was medium, it can be inferred that 17α-ethinylestradiol has a lower risk than the calculated for its concentration. Also, an acceptable incremental lifetime carcinogenic risk was observed for distillate.

The use of the YES assay combined with detection and identification of micropollutants allowed an effective assessment of the overall treatment performance and demonstrated the ability of the AnOMBR-MD to reduce environmental and human health risks in a great extent.

Acknowledgments

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References

[1] B. Tiwari, B. Sellamuthu, Y. Ouarda, P. Drogui, R.D. Tyagi, G. Buelna, Review on fate and mechanism of removal of pharmaceutical pollutants from wastewater using biological approach, Bioresource Technology. 224 (2017) 1–12. https://doi.org/10.1016/j.biortech.2016.11.042.

[2] T. aus der Beek, F.-A. Weber, A. Bergmann, G. Grüttner, A. Carius, Pharmaceuticals in the environment: Global occurrence and potential cooperative action under the Strategic Approach to International Chemicals Management (SAICM), Umweltbundesamt, 2016. https://www.umweltbundesamt.de/publikationen/pharmaceuticals-in-the-environment-global (accessed July 14, 2020).

[3] Å. Bergman, J.J. Heindel, S. Jobling, J.A. Kidd, R.T. Zoeller, State of the science of endocrine disrupting chemicals - 2012 an assessment of the state of the science of endocrine

disruptors, WHO ; UNEP, Geneva, 2013. http://www.who.int/ceh/publications/endocrine/en/index.html (accessed August 19, 2017).

[4] E.R. Kabir, M.S. Rahman, I. Rahman, A review on endocrine disruptors and their possible impacts on human health, Environmental Toxicology and Pharmacology. 40 (2015) 241–258. https://doi.org/10.1016/j.etap.2015.06.009.

[5] L.C. Folmar, M.J. Hemmer, N.D. Denslow, K. Kroll, J. Chen, A. Cheek, H. Richman, H. Meredith, E.G. Grau, A comparison of the estrogenic potencies of estradiol, ethynylestradiol, diethylstilbestrol, nonylphenol and methoxychlor in vivo and in vitro, Aquatic Toxicology. 60 (2002) 101–110. https://doi.org/10.1016/S0166-445X(01)00276-4.

[6] J.A. McLachlan, E. Simpson, M. Martin, Endocrine disrupters and female reproductive health, Best Practice & Research Clinical Endocrinology & Metabolism. 20 (2006) 63–75. https://doi.org/10.1016/j.beem.2005.09.009.

[7] E.P. Costa, M. Roccamante, P. Plaza-Bolaños, I. Oller, A. Agüera, C.C. Amorim, S. Malato, Aluminized surface to improve solar light absorption in open reactors: Application for micropollutants removal in effluents from municipal wastewater treatment plants, Science of The Total Environment. 755 (2021) 142624. https://doi.org/10.1016/j.scitotenv.2020.142624.

[8] T. Fundneider, V. Acevedo Alonso, A. Wick, D. Albrecht, S. Lackner, Implications of biological activated carbon filters for micropollutant removal in wastewater treatment, Water Research. 189 (2021) 116588. https://doi.org/10.1016/j.watres.2020.116588.

[9] C.-H. Wei, C. Hoppe-Jones, G. Amy, T. Leiknes, Organic micro-pollutants' removal via anaerobic membrane bioreactor with ultrafiltration and nanofiltration, Journal of Water Reuse and Desalination. 6 (2016) 362–370. https://doi.org/10.2166/wrd.2015.138.

[10] Y. Kim, S. Li, L. Chekli, Y.C. Woo, C.-H. Wei, S. Phuntsho, N. Ghaffour, T. Leiknes, H.K. Shon, Assessing the removal of organic micro-pollutants from anaerobic membrane bioreactor effluent by fertilizer-drawn forward osmosis, Journal of Membrane Science. 533 (2017) 84–95. https://doi.org/10.1016/j.memsci.2017.03.027.

[11] P.Y. Kunz, C. Kienle, M. Carere, N. Homazava, R. Kase, In vitro bioassays to screen for endocrine active pharmaceuticals in surface and waste waters, Journal of Pharmaceutical and Biomedical Analysis. 106 (2015) 107–115. https://doi.org/10.1016/j.jpba.2014.11.018.

[12] F.D.L. Leusch, C. de Jager, Y. Levi, R. Lim, L. Puijker, F. Sacher, L.A. Tremblay, V.S. Wilson, H.F. Chapman, Comparison of Five in Vitro Bioassays to Measure Estrogenic Activity in Environmental Waters, Environmental Science & Technology. 44 (2010) 3853–3860. https://doi.org/10.1021/es903899d.

[13] M. Wieczerzak, B. Kudłak, G. Yotova, M. Nedyalkova, S. Tsakovski, V. Simeonov, J. Namieśnik, Modeling of pharmaceuticals mixtures toxicity with deviation ratio and best-fit functions models, Science of The Total Environment. 571 (2016) 259–268. https://doi.org/10.1016/j.scitotenv.2016.07.186.

[14] O.L. de V. María Teresa, A.-L. Jessica, Y.-N. Isaura, Assessing the Estrogenic Activity of EDCs and Human Risks of Groundwater after Ozonation and Chlorination, Ozone: Science & Engineering. 42 (2020) 244–254. https://doi.org/10.1080/01919512.2019.1653753.

[15] K. Eichbaum, M. Brinkmann, S. Buchinger, G. Reifferscheid, M. Hecker, J.P. Giesy, M. Engwall, B. van Bavel, H. Hollert, In vitro bioassays for detecting dioxin-like activity —

Application potentials and limits of detection, a review, Science of The Total Environment. 487 (2014) 37–48. https://doi.org/10.1016/j.scitotenv.2014.03.057.

[16] E.J. Routledge, J.P. Sumpter, Estrogenic activity of surfactants and some of their degradation products assessed using a recombinant yeast screen, Environmental Toxicology and Chemistry. 15 (1996) 241–248.

[17] P. Verlicchi, M. Al Aukidy, E. Zambello, Occurrence of pharmaceutical compounds in urban wastewater: Removal, mass load and environmental risk after a secondary treatment—A review, Science of The Total Environment. 429 (2012) 123–155. https://doi.org/10.1016/j.scitotenv.2012.04.028.

[18] X. Wang, V.W.C. Chang, C.Y. Tang, Osmotic membrane bioreactor (OMBR) technology for wastewater treatment and reclamation: Advances, challenges, and prospects for the future, Journal of Membrane Science. 504 (2016) 113–132. https://doi.org/10.1016/j.memsci.2016.01.010.

[19] R.W. Holloway, A.S. Wait, A. Fernandes da Silva, J. Herron, M.D. Schutter, K. Lampi, T.Y. Cath, Long-term pilot scale investigation of novel hybrid ultrafiltration-osmotic membrane bioreactors, Desalination. 363 (2015) 64–74. https://doi.org/10.1016/j.desal.2014.05.040.

[20] A. Achilli, T.Y. Cath, A.E. Childress, Selection of inorganic-based draw solutions for forward osmosis applications, Journal of Membrane Science. 364 (2010) 233–241. https://doi.org/10.1016/j.memsci.2010.08.010.

[21] T. Stephenson, K. Brindle, S. Judd, B. Jefferson, Membrane Bioreactors for Wastewater Treatment, 1st ed., IWA Publishing, London, UK, 2000.

[22] S. Judd, C. Judd, The MBR book: principles and applications of membrane bioreactors in water and wastewater treatment, 1st ed, Elsevier, Amsterdam ; Boston, 2006.

[23] G. Qiu, S. Zhang, D.S. Srinivasa Raghavan, S. Das, Y.-P. Ting, The potential of hybrid forward osmosis membrane bioreactor (FOMBR) processes in achieving high throughput treatment of municipal wastewater with enhanced phosphorus recovery, Water Research. 105 (2016) 370–382. https://doi.org/10.1016/j.watres.2016.09.017.

[24] B.C. Ricci, B. Skibinski, K. Koch, C. Mancel, C.Q. Celestino, I.L.C. Cunha, M.R. Silva, C.B. Alvim, C.V. Faria, L.H. Andrade, L.C. Lange, M.C.S. Amaral, Critical performance assessment of a submerged hybrid forward osmosis - membrane distillation system, Desalination. 468 (2019) 114082. https://doi.org/10.1016/j.desal.2019.114082.

[25] L. Zohrabian, N.P. Hankins, R.W. Field, Hybrid forward osmosis-membrane distillation system: Demonstration of technical feasibility, Journal of Water Process Engineering. 33 (2020) 101042. https://doi.org/10.1016/j.jwpe.2019.101042.

[26] Y. Wu, X. Wang, M.Q.X. Tay, S. Oh, L. Yang, C. Tang, B. Cao, Metagenomic insights into the influence of salinity and cytostatic drugs on the composition and functional genes of microbial community in forward osmosis anaerobic membrane bioreactors, Chemical Engineering Journal. 326 (2017) 462–469. https://doi.org/10.1016/j.cej.2017.05.172.

[27] S.F. de Aquino, E.M.F. Brandt, C.A. de L. Chernicharo, Remoção de fármacos e desreguladores endócrinos em estações de tratamento de esgoto: revisão da literatura, Engenharia Sanitária e Ambiental. 18 (2013) 187–204. https://doi.org/10.1590/S1413-41522013000300002.

[28] A.V. Santos, C.F. Couto, Y.A. Lebron, V.R. Moreira, A.F.S. Foureaux, E.O. Reis, L.V. de Souza Santos, L.H. de Andrade, M.C.S. Amaral, L.C. Lange, Occurrence and risk

assessment of pharmaceutically active compounds in water supply systems in Brazil, Science of The Total Environment. (2020) 141011. https://doi.org/10.1016/j.scitotenv.2020.141011.

[29] E.O. Reis, A.F.S. Foureaux, J.S. Rodrigues, V.R. Moreira, Y.A.R. Lebron, L.V.S. Santos, M.C.S. Amaral, L.C. Lange, Occurrence, removal and seasonal variation of pharmaceuticals in Brasilian drinking water treatment plants, Environmental Pollution. 250 (2019) 773–781. https://doi.org/10.1016/j.envpol.2019.04.102.

[30] C.-N. Chang, Y.-S. Ma, C.-W. Lo, Application of oxidation–reduction potential as a controlling parameter in waste activated sludge hydrolysis, Chemical Engineering Journal. 90 (2002) 273–281. https://doi.org/10.1016/S1385-8947(02)00015-3.

[31] APHA, Standard Methods for the Examination of Water and Wastewater, 23rd ed., APHA, AWWA, WPCF, New York, 2017.

[32] H. Kapp, Schlammfaulung mit hohem Feststoffgehalt, Kommissionsverlag Oldenbourg, 1984. http://agris.fao.org/agris-search/search.do?recordID=US201300384705 (accessed February 4, 2020).

[33] C.V. Faria, B.C. Ricci, A.F.R. Silva, M.C.S. Amaral, F.V. Fonseca, Removal of micropollutants in domestic wastewater by expanded granular sludge bed membrane bioreactor, Process Safety and Environmental Protection. 136 (2020) 223–233. https://doi.org/10.1016/j.psep.2020.01.033.

[34] A. Klindworth, E. Pruesse, T. Schweer, J. Peplies, C. Quast, M. Horn, F.O. Glöckner, Evaluation of general 16S ribosomal RNA gene PCR primers for classical and next-generation sequencing-based diversity studies, Nucleic Acids Res. 41 (2013) e1. https://doi.org/10.1093/nar/gks808.

[35] V.S. Pylro, L.F.W. Roesch, J.M. Ortega, A.M. do Amaral, M.R. Tótola, P.R. Hirsch, A.S. Rosado, A. Góes-Neto, A.L. da Costa da Silva, C.A. Rosa, D.K. Morais, F.D. Andreote, G.F. Duarte, I.S. de Melo, L. Seldin, M.R. Lambais, M. Hungria, R.S. Peixoto, R.H. Kruger, S.M. Tsai, V. Azevedo, The Brazilian Microbiome Project Organization Committee, Brazilian Microbiome Project: Revealing the Unexplored Microbial Diversity—Challenges and Prospects, Microb Ecol. 67 (2014) 237–241. https://doi.org/10.1007/s00248-013-0302-4.

[36] J.G. Caporaso, J. Kuczynski, J. Stombaugh, K. Bittinger, F.D. Bushman, E.K. Costello, N. Fierer, A.G. Peña, J.K. Goodrich, J.I. Gordon, G.A. Huttley, S.T. Kelley, D. Knights, J.E. Koenig, R.E. Ley, C.A. Lozupone, D. McDonald, B.D. Muegge, M. Pirrung, J. Reeder, J.R. Sevinsky, P.J. Turnbaugh, W.A. Walters, J. Widmann, T. Yatsunenko, J. Zaneveld, R. Knight, QIIME allows analysis of high-throughput community sequencing data, Nature Methods. 7 (2010) 335–336. https://doi.org/10.1038/nmeth.f.303.

[37] M.T.L. do Nascimento, A.D. de O. Santos, L.C. Felix, G. Gomes, M. de Oliveira e Sá, D.L. da Cunha, N. Vieira, R.A. Hauser-Davis, J.A. Baptista Neto, D.M. Bila, Determination of water quality, toxicity and estrogenic activity in a nearshore marine environment in Rio de Janeiro, Southeastern Brazil, Ecotoxicology and Environmental Safety. 149 (2018) 197–202. https://doi.org/10.1016/j.ecoenv.2017.11.045.

[38] D. Bila, A.F. Montalvão, D. de A. Azevedo, M. Dezotti, Estrogenic activity removal of 17β-estradiol by ozonation and identification of by-products, Chemosphere. 69 (2007) 736–746. https://doi.org/10.1016/j.chemosphere.2007.05.016.

[39] J.T. Landis, H. An, A.G. Bailey, D.P. Dittmer, J.S. Marron, CRAN - Package “dr4pl,” (2019). https://cran.r-project.org/web/packages/topsis/index.html (accessed November 15, 2019).

[40] R Core Team, R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing. Versão 3.2.1, (2015). https://www.r-project.org/ (accessed November 9, 2017).

[41] US EPA, Definition and procedure for the determination of the method detection limit, Revision 2., (2016). https://www.epa.gov/sites/production/files/2016-12/documents/mdl-procedure_rev2_12-13-2016.pdf (accessed January 27, 2020).

[42] INMETRO, DOQ-CGCRE-008. Orientação sobre validação de métodos de ensaios químicos., Instituto Nacional de Metrologia, Normalização e Qualidade Industrial, Rio de Janeiro, 2016. http://www.inmetro.gov.br/Sidoq/Arquivos/Cgcre/DOQ/DOQ-Cgcre-8_05.pdf (accessed October 15, 2019).

[43] C.M. Johnson, M. Achary, R.P. Suri, An Interaction Model for Estimating In Vitro Estrogenic and Androgenic Activity of Chemical Mixtures, Environmental Science & Technology. 47 (2013) 4661–4669. https://doi.org/10.1021/es304939c.

[44] European Commission, ed., Technical guidance document in support of Commission directive 93 67 EEC on risk assessment for new notified substances and Commission regulation (EC) no. 1488 94 on risk assessment for existing substances., Office for Official Publ. of the European Communities, Luxembourg, 1996.

[45] WHO, Guidelines for drinking-water quality., 4th ed., World Health Organization, Geneva, 2017.

[46] US EPA, Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures, (2000). https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=20533 (accessed July 6, 2020).

[47] US EPA, Risk Assessment Guidance for Superfund (RAGS) Volume III: Part A, US EPA. (2015). https://www.epa.gov/risk/risk-assessment-guidance-superfund-rags-volume-iii-part (accessed June 22, 2020).

[48] California EPA, Expedited Cancer Potency Values and Proposed Regulatory levels for certain proposition 65 carcinogens (Reproductive and cancer hazard assessment section), (1992). https://oehha.ca.gov/media/downloads/proposition-65/report/expcancer.pdf.

[49] F. Riva, S. Castiglioni, E. Fattore, A. Manenti, E. Davoli, E. Zuccato, Monitoring emerging contaminants in the drinking water of Milan and assessment of the human risk, International Journal of Hygiene and Environmental Health. 221 (2018) 451–457. https://doi.org/10.1016/j.ijheh.2018.01.008.

[50] X. Wang, C. Wang, C.Y. Tang, T. Hu, X. Li, Y. Ren, Development of a novel anaerobic membrane bioreactor simultaneously integrating microfiltration and forward osmosis membranes for low-strength wastewater treatment, Journal of Membrane Science. 527 (2017) 1–7. https://doi.org/10.1016/j.memsci.2016.12.062.

[51] F. Volpin, L. Chekli, S. Phuntsho, N. Ghaffour, J.S. Vrouwenvelder, H.K. Shon, Optimisation of a forward osmosis and membrane distillation hybrid system for the treatment of source-separated urine, Separation and Purification Technology. 212 (2019) 368–375. https://doi.org/10.1016/j.seppur.2018.11.003.

[52] W. Luo, F.I. Hai, W.E. Price, W. Guo, H.H. Ngo, K. Yamamoto, L.D. Nghiem, Phosphorus and water recovery by a novel osmotic membrane bioreactor–reverse osmosis system, Bioresource Technology. 200 (2016) 297–304. https://doi.org/10.1016/j.biortech.2015.10.029.

[53] A.J. Ansari, F.I. Hai, W. Guo, H.H. Ngo, W.E. Price, L.D. Nghiem, Selection of forward osmosis draw solutes for subsequent integration with anaerobic treatment to facilitate resource recovery from wastewater, Bioresource Technology. 191 (2015) 30–36. https://doi.org/10.1016/j.biortech.2015.04.119.

[54] A.M. Bacaksiz, Y. Kaya, C. Aydiner, Techno-economic preferability of cost−performance effective draw solutions for forward osmosis and osmotic anaerobic bioreactor applications, Chemical Engineering Journal. (2020) 127535. https://doi.org/10.1016/j.cej.2020.127535.

[55] M. Ramezanianpour, M. Sivakumar, An analytical flux decline model for membrane distillation, Desalination. 345 (2014) 1–12. https://doi.org/10.1016/j.desal.2014.04.006.

[56] Y. Zhang, J. Geng, H. Ma, H. Ren, K. Xu, L. Ding, Characterization of microbial community and antibiotic resistance genes in activated sludge under tetracycline and sulfamethoxazole selection pressure, Science of The Total Environment. 571 (2016) 479–486. https://doi.org/10.1016/j.scitotenv.2016.07.014.

[57] M. Huang, F. Qi, J. Wang, Q. Xu, L. Lin, Changes of bacterial diversity and tetracycline resistance in sludge from AAO systems upon exposure to tetracycline pressure, Journal of Hazardous Materials. 298 (2015) 303–309. https://doi.org/10.1016/j.jhazmat.2015.05.039.

[58] C. Jiang, J. Geng, H. Hu, H. Ma, X. Gao, H. Ren, Impact of selected non-steroidal anti-inflammatory pharmaceuticals on microbial community assembly and activity in sequencing batch reactors, PLoS ONE. 12 (2017) e0179236. https://doi.org/10.1371/journal.pone.0179236.

[59] S. Chen, H. Cheng, K.N. Wyckoff, Q. He, Linkages of Firmicutes and Bacteroidetes populations to methanogenic process performance, J Ind Microbiol Biotechnol. 43 (2016) 771–781. https://doi.org/10.1007/s10295-016-1760-8.

[60] J.D. Muñoz Sierra, W. Wang, D. Cerqueda-Garcia, M.J. Oosterkamp, H. Spanjers, J.B. van Lier, Temperature susceptibility of a mesophilic anaerobic membrane bioreactor treating saline phenol-containing wastewater, Chemosphere. 213 (2018) 92–102. https://doi.org/10.1016/j.chemosphere.2018.09.023.

[61] S. Wang, X. Hou, H. Su, Exploration of the relationship between biogas production and microbial community under high salinity conditions, Sci Rep. 7 (2017) 1149. https://doi.org/10.1038/s41598-017-01298-y.

[62] T. Narihiro, M.K. Nobu, B.T.W. Bocher, R. Mei, W.-T. Liu, Co-occurrence network analysis reveals thermodynamics-driven microbial interactions in methanogenic bioreactors: Thermodynamics-driven microbial interactions, Environmental Microbiology Reports. 10 (2018) 673–685. https://doi.org/10.1111/1758-2229.12689.

[63] L. Hao, A. Bize, D. Conteau, O. Chapleur, S. Courtois, P. Kroff, E. Desmond-Le Quéméner, T. Bouchez, L. Mazéas, New insights into the key microbial phylotypes of anaerobic sludge digesters under different operational conditions, Water Research. 102 (2016) 158–169. https://doi.org/10.1016/j.watres.2016.06.014.

[64] R. Chouari, D. Le Paslier, P. Daegelen, P. Ginestet, J. Weissenbach, A. Sghir, Molecular Evidence for Novel Planctomycete Diversityin a Municipal Wastewater TreatmentPlant, AEM. 69 (2003) 7354–7363. https://doi.org/10.1128/AEM.69.12.7354-7363.2003.

[65] J.A. Fuerst, E. Sagulenko, Beyond the bacterium: planctomycetes challenge our concepts of microbial structure and function, Nat Rev Microbiol. 9 (2011) 403–413. https://doi.org/10.1038/nrmicro2578.

[66] E.C. Symsaris, I.A. Fotidis, A.S. Stasinakis, I. Angelidaki, Effects of triclosan, diclofenac, and nonylphenol on mesophilic and thermophilic methanogenic activity and on the methanogenic communities, Journal of Hazardous Materials. 291 (2015) 45–51. https://doi.org/10.1016/j.jhazmat.2015.03.002.

[67] Y. Abner Rocha Lebron, P. Barbosa Moser, V. Rezende Moreira, G. Rodrigues dos Anjos Silva, A. Soalheiro, B. Pimenta de Souza, E. Coutinho de Paula, M. Cristina Santos Amaral, Osmotic membrane bioreactor (OMBR) in refinery wastewater treatment: The impact of a draw solute with lower diffusivity in the process performance, Chemical Engineering Journal. 406 (2021) 127074. https://doi.org/10.1016/j.cej.2020.127074.

[68] K. Kundu, S. Sharma, T.R. Sreekrishnan, Effect of operating temperatures on the microbial community profiles in a high cell density hybrid anaerobic bioreactor, Bioresource Technology. 118 (2012) 502–511. https://doi.org/10.1016/j.biortech.2012.05.047.

[69] K. Fent, C. Escher, D. Caminada, Estrogenic activity of pharmaceuticals and pharmaceutical mixtures in a yeast reporter gene system, Reproductive Toxicology. 22 (2006) 175–185. https://doi.org/10.1016/j.reprotox.2006.04.010.

[70] M. Isidori, M. Bellotta, M. Cangiano, A. Parrella, Estrogenic activity of pharmaceuticals in the aquatic environment, Environment International. 35 (2009) 826–829. https://doi.org/10.1016/j.envint.2008.11.006.

[71] R. Kanda, J. Churchley, Removal of endocrine disrupting compounds during conventional wastewater treatment, Environmental Technology. 29 (2008) 315–323. https://doi.org/10.1080/09593330802099874.

[72] T. Smital, S. Terzic, R. Zaja, I. Senta, B. Pivcevic, M. Popovic, I. Mikac, K.E. Tollefsen, K.V. Thomas, M. Ahel, Assessment of toxicological profiles of the municipal wastewater effluents using chemical analyses and bioassays, Ecotoxicology and Environmental Safety. 74 (2011) 844–851. https://doi.org/10.1016/j.ecoenv.2010.11.010.

[73] P.R. da Silva, A.H. Mounteer, L. dos Anjos Benjamin, E.R. de Almeida, F.B. Vitorino, G.S. Arcanjo, V. Rodrigues dos Santos Petersen, Evaluation of toxicity and estrogenicity in UASB - treated municipal sewage, Chemosphere. (2020) 128778. https://doi.org/10.1016/j.chemosphere.2020.128778.

[74] C.P. Czajka, K.L. Londry, Anaerobic biotransformation of estrogens, Science of The Total Environment. 367 (2006) 932–941. https://doi.org/10.1016/j.scitotenv.2006.01.021.

[75] T.Z.D. des Mes, K. Kujawa-Roeleveld, G. Zeeman, G. Lettinga, Anaerobic biodegradation of estrogens—hard to digest, Water Science and Technology. 57 (2008) 1177–1182. https://doi.org/10.2166/wst.2008.102.

[76] C. Grandclément, I. Seyssiecq, A. Piram, P. Wong-Wah-Chung, G. Vanot, N. Tiliacos, N. Roche, P. Doumenq, From the conventional biological wastewater treatment to hybrid processes, the evaluation of organic micropollutant removal: A review, Water Research. 111 (2017) 297–317. https://doi.org/10.1016/j.watres.2017.01.005.

[77] C. Prasse, D. Stalter, U. Schulte-Oehlmann, J. Oehlmann, T.A. Ternes, Spoilt for choice: A critical review on the chemical and biological assessment of current wastewater treatment technologies, Water Research. 87 (2015) 237–270. https://doi.org/10.1016/j.watres.2015.09.023.

[78] N. Paterakis, T.Y. Chiu, Y.K.K. Koh, J.N. Lester, E.J. McAdam, M.D. Scrimshaw, A. Soares, E. Cartmell, The effectiveness of anaerobic digestion in removing estrogens and nonylphenol ethoxylates, Journal of Hazardous Materials. 199–200 (2012) 88–95. https://doi.org/10.1016/j.jhazmat.2011.10.075.

[79] K. Wille, H. Noppe, K. Verheyden, J. Vanden Bussche, E. De Wulf, P. Van Caeter, C.R. Janssen, H.F. De Brabander, L. Vanhaecke, Validation and application of an LC-MS/MS method for the simultaneous quantification of 13 pharmaceuticals in seawater, Anal Bioanal Chem. 397 (2010) 1797–1808. https://doi.org/10.1007/s00216-010-3702-z.

[80] C.W. Muriuki, P.G. Home, J.M. Raude, E.K. Ngumba, G.K. Munala, P.K. Kairigo, A.N. Gachanja, T.A. Tuhkanen, Occurrence, distribution, and risk assessment of pharmerciuticals in wastewater and open surface drains of peri-urban areas: Case study of Juja town, Kenya, Environmental Pollution. 267 (2020) 115503. https://doi.org/10.1016/j.envpol.2020.115503.

[81] D. Ramírez-Morales, M. Masís-Mora, J.R. Montiel-Mora, J.C. Cambronero-Heinrichs, S. Briceño-Guevara, C.E. Rojas-Sánchez, M. Méndez-Rivera, V. Arias-Mora, R. Tormo-Budowski, L. Brenes-Alfaro, C.E. Rodríguez-Rodríguez, Occurrence of pharmaceuticals, hazard assessment and ecotoxicological evaluation of wastewater treatment plants in Costa Rica, Science of The Total Environment. 746 (2020) 141200. https://doi.org/10.1016/j.scitotenv.2020.141200.

[82] S.-S. Cao, Y.-P. Duan, Y.-J. Tu, Y. Tang, J. Liu, W.-D. Zhi, C. Dai, Pharmaceuticals and personal care products in a drinking water resource of Yangtze River Delta Ecology and Greenery Integration Development Demonstration Zone in China: Occurrence and human health risk assessment, Science of The Total Environment. 721 (2020) 137624. https://doi.org/10.1016/j.scitotenv.2020.137624.

[83] S.Y. Wee, D.E.M. Haron, A.Z. Aris, F.Md. Yusoff, S.M. Praveena, Active pharmaceutical ingredients in Malaysian drinking water: consumption, exposure, and human health risk, Environ Geochem Health. 42 (2020) 3247–3261. https://doi.org/10.1007/s10653-020-00565-8.

Chapter 2: Draw solution solute selection for a hybrid forward osmosis-membrane distillation module: effects on trace organic compound rejection, water flux and polarization

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Draw solution solute selection for a hybrid forward osmosis-membrane distillation module: Effects on trace organic compound rejection, water flux and polarization

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Abstract: The integrated forward osmosis membrane bioreactor and membrane distillation (OMBR-MD) is an emerging technique for wastewater reclamation and trace organic compound (TrOC) removal. The selection of draw solution (DS) for this system should consider the particularities of both forward osmosis and membrane distillation. The effect of five different draw solutions on forward osmosis and TrOC rejection in a hybrid submerged forward osmosis - membrane distillation (FO-MD) module was investigated in this study. The roles of each solution on FO and MD water flux, FO reverse salt flux, temperature, concentration polarization and rejection of 7 TrOCs were explored. The salt used in the draw solution influenced both FO water flux (NaCl = $MgOAc_2$ (4.8 $L.m^{-2}.h^{-1}$) > NaOAc (4.6 $L.m^{-2}.h^{-1}$) > $MgCl_2$ (3.6 $L.m^{-2}.h^{-1}$) > $EDTA\text{-}Na_2$ (2.8 $L.m^{-2}.h^{-1}$)) and MD water flux (NaOAc (4.0 $L.m^{-2}.h^{-1}$) > NaCl (3.8 $L.m^{-2}.h^{-1}$) > $MgCl_2$ (3.3 $L.m^{-2}.h^{-1}$) > $MgOAc_2$ (3.1 $L.m^{-2}.h^{-1}$> $EDTA\text{-}Na_2$ (3.0 $L.m^{-2}.h^{-1}$)). $MgCl_2$ draw solution produced the lowest FO reverse salt flux, demonstrating its potential to prevent salinity build-up when applied in OMBR-MD. $MgCl_2$ and NaCl were the only salts completely rejected by the distillation membrane, which prevents salt losses during draw solution reconcentration. Regardless of the draw solution salt, the integrated FO-MD module could effectively remove 6 of the 7 TrOCs. $MgCl_2$ and NaOAc afforded the highest TrOC rejections, while the lowest rejections were observed when $MgAOc_2$ was used. $MgCl_2$ was selected as the best DS salt for OMBR-MD by using the technique for order preference by similarity to ideal solution (TOPSIS) tool.

Keywords: micropollutants; reverse salt flux; wastewater treatment; multicriteria decision making; concentration polarization.

1 Introduction

Membrane bioreactors (MBRs) have gained attention in recent years for treatment of urban sewage given the inherent benefits of biological treatment, allied with the high solids contents found in these reactors, which improves organic matter and nutrient removal [1,2]. Integration of the MBR with forward osmosis (FO) in the osmotic membrane bioreactor (OMBR) is an emerging technology that can overcome disadvantages of MBRs, such as lower tendency to fouling that will lead to lower energy demands [3]. FO affords high rejection of dissolved compounds because it uses nonporous membranes and therefore OMBRs are an interesting alternative for treatment of wastewaters that contain recalcitrant organic compounds [4,5]. Removal efficiencies of over 90% have been reported in the literature, with most recalcitrant compounds below their detection limits [6,7].

In FO water passes from a low osmotic pressure feed solution to a high osmotic pressure draw solution (DS) through a semipermeable membrane [8,9]. The FO driving force is the osmotic pressure difference between feed and DS, without the need for a hydraulic pressure, which reduces energy consumption and fouling tendency [10].

When water passes through the FO membrane the DS is diluted, but to guarantee process efficiency the osmotic pressure of the DS (π_{DS}) must be kept constant, causing the need for a process that recovers treated water while maintaining stable FO flux [9]. Membrane assisted distillation (MD) is a separation process whose driving force is vapor pressure difference (ΔP_v). In MD, volatile compounds pass through the microporous hydrophobic distillation membrane while nonvolatile compounds are rejected [11]. MD is not affected by feed solution salinity and therefore has a good potential for DS regeneration.

An integrated FO-MD process combines advantages of both membrane processes for wastewater treatment, draw solution regeneration and production of high-quality reuse water. To integrate FO with MD it is necessary to develop a synergistic permeate flux balance for both FO and MD membranes. The integration of FO and MD has been investigated by various authors [12–18]. However, only Husnain et al. [12] and Ricci et al. [18] used a hybrid FO-MD module. Husnain et al. [12] used an external module for treatment of synthetic wastewater with NaCl as DS salt. The authors reported complete removal of COD and TSS with higher FO fluxes when the DS was at higher temperature. Ricci et al. [18] described a novel submerged FO-MD module with NaCl as DS salt for domestic sewage treatment and concluded that the

hybrid module had a lower energy demand than individual FO and MD modules, and yielded over 97.5% rejection of micropollutants [18].

DS salt selection is a key point for the OMBR since the salt used will affect microbial metabolism and thus process performance. The DS salt should have high solubility, diffusivity and osmotic pressure and low molar mass, viscosity, reverse salt flux (J_s) and cost and should be easily reconcentrated [19–22]. Beyond these aspects, some studies have demonstrated that the salt influences micropollutant rejection in FO [23–25], which should be taken into account in its selection.

For integration of the OMBR with MD, criteria beyond those mentioned for FO must be considered. Given that the driving force of MD is $\Delta P_{v,}$ the salt used should have minimal effect on DS vapor pressure [26]. Furthermore, salt solubility is an important factor for MD since temperature and concentration polarization can cause salt precipitation on the membrane surface and consequently membrane fouling and reduced permeate flow. Differently from FO, the salt should have low diffusivity to reduce concentration polarization and should not be volatile. Additionally, DS temperature, which should be elevated, has a great impact on FO and on solubility. In light of the above, DS salts should not be evaluated for FO and MD processes separately.

Performance of different salts (NaCl, $MgCl_2$, sodium acetate, magnesium acetate, EDTA-Na_2, among others) has been previously evaluated [27–30], as have salt mixtures for FO and MBR [22]. Only two studies compared different salts in integrated OMBR-MD [15,26], however both used individual membrane modules, with heated DS only in feed to the MD module. DS temperature was not adjusted in any of the studies since the FO and MD processes were not coupled. Thus, salt performance, polarization and micropollutant removal still need to be investigated in a submerged hybrid FO-MD module, for future incorporation into an OMBR-MD system.

Since OMBR-MD salt selection depends on the several previously mentioned criteria, a multicriteria decision making is a useful analysis. TOPSIS (technique for order preference by similarity to ideal solution) is one of the most widely used multicriteria decision making when information on attributes is available on cardinal scale [31]. TOPSIS is based on the concept that the best alternative is that which is closest to the ideal positive solution and furthest from the ideal negative solution [32]. The positive ideal solution is a hypothetical scenario that has the best values for all the considered criteria and, on the contrary, the negative ideal solution is the one with the worst values [33]. TOPSIS was used for several researchers to support decision

making in wastewater treatment technology selection [32], water treatment [34], emergency water technology [35], water resource decision making [36], water distribution systems [37] and municipal solid waste planning [38].

Hence, for the first time, at the present paper, the performance of five different salts in a FO-MD integrated in just one submerged hybrid module was evaluated, with regard to process polarizations and rejection of seven pharmaceutical drugs (17α-ethinylestradiol, betamethasone, ketoprofen, fenofibrate, fluconazole, loratadine and prednisone). The TOPSIS multicriteria decision making technique was used to select the best salt for an OMBR-MD system.

It should be noted that FO-MD systems reported in the literature are nonuniform, making selection of the best DS more difficult [17,39]. Therefore, operating conditions (osmotic pressure, circulation velocity, DS and distillate temperatures) and membrane types were not modified throughout the evaluation to improve comparison among salts.

2 Material and methods

2.1 Chemicals and solutions

2.1.1 Draw solutions

Sodium chloride (NaCl), sodium acetate (NaOAc), magnesium acetate ($MgOAc_2$) and ethylenediaminetetraacetic acid disodium salt (EDTA-Na_2) salts were purchased from Neon (Suzano, São Paulo, Brazil). Magnesium chloride ($MgCl_2$) was purchased from Êxodo (Sumaré, São Paulo, Brazil). NaCl was chosen because it is the most used solute to compose draw solution in FO process [21]. $MgCl_2$, NaOAc and $MgOAc_2$ were the most suitable solutes for FO applications in two studies [27,29]. And EDTA-Na_2 has been demonstrated as an excellent draw solution since it has high osmotic pressure and low reverse salt flux [40].

All draw solutions were prepared with deionized water at concentrations with osmotic pressures of 28 bar (Table 1). Osmotic pressure ($\pi_{DS,b}$) was calculated by the Morse equation (Eq. (1)), derived from the Van't Hoff equation:

$$\pi = iMRT \qquad (1)$$

in which i is the Van't Hoff factor (Table 1) for each solute, M is the solute molar concentration, R is the universal gas constant (8.314 x 10^{-2} L.bar.mol^{-1}.K^{-1}) and T is the absolute temperature [19].

Table 1 - Van't Hoff factor and draw solution concentration (C_{DS}) required to generate an osmotic pressure of 28 bar at 45 °C

Draw solute	Van't Hoff factor (*i*)	M_{DS} (mol.L^{-1})	C_{DS} (g.L^{-1})	Reference
NaCl	1.844	0.57	33.54	[27]
$MgCl_2$	2.962	0.36	34.02	[41]
NaOAc	1.681	0.63	51.66	[28]
$MgOAc_2$	1.345	0.79	112.07	[28]
EDTA-Na_2	4.034	0.26	88.23	[28]

2.1.2 Trace organic compounds

17α-ethinylestradiol (EE2), betamethasone (BET), fenofibrate (FEN), fluconazole (FLU), ketoprofen (KET), loratadine (LOR) and prednisone (PRE) were chosen as trace organic compound (TrOC) (Table 2) in this study because they have been found in domestic wastewater, surface, ground and drinking water in Brazil [42–45]. The 7 TrOC were purchased from Sigma Aldrich (Cotia, São Paulo, Brazil) and stock solutions (2 mg.L^{-1}) of each were prepared in pure methanol (Sigma Aldrich). Molecular structure of the 7 TrOC is presented in Table S1 (supplementary material – Appendix B).

Table 2 - Physicochemical properties of TrOC used in feed solution

TrOC	MW (g.mol^{-1})	Log K_{ow}	pK_a	pK_H	DL[a] (ng.L^{-1})
17α-Ethynilestradiol	296.41	3.9	-1.66 and 10.33	11.09	69.49
Betamethasone	392.47	1.68	12.42	7.14	2.75
Fenofibrate	254.28	3.61	3.88	8.34	0.67
Fluconazole	360.83	5.28	-	12.98	0.90
Ketoprofen	306.28	0.56	2.3 and 12.68	10.67	0.44
Loratadine	382.89	4.55	4.33	12.49	0.59
Prednisone	358.43	1.66	12.68	9.54	1.11

[a]Detection limit for liquid chromatograph - mass spectrometry.
(Source: Ricci et al. [18]).

2.2 Membranes

A flat-sheet FO membrane manufactured by Fluid Technology Solutions (FTSH2O™, Albany, OR, USA) was purchased from Sterlitech Corporation (Kent, USA). The asymmetric

cellulose triacetate (CTA) membrane had a 707 μm structure parameter (S) [46]; tests were performed with the active layer facing the feed solution (AL-FS). A flat-sheet MD membrane with an average pore size of 0.2 μm was also purchased from Sterlitech Corporation (Kent, USA). It was a polytetrafluoroethylene (PTFE) membrane laminated on a polypropylene layer; tests were conducted in a direct contact configuration (DC-MD).

2.3 FO membrane permeability characterization

The FO membrane was tested in reverse osmosis (RO) mode for FO membrane permeability characterization using a pressurized cross-flow filtration cell [47]. The water permeability coefficient (A) was obtained from deionized water flux over applied pressure differences ranging from 13 bar to 5 bar, at 2 bar intervals [48]. Temperature was held constant at 25 °C. Water permeability at the DS temperature (T) was corrected by the ratio of water viscosity (μ) at T and 25 °C (Eq. (2)).

$$A_T = \frac{\mu_{25}}{\mu_T} \times A_{25} \qquad (2)$$

2.4 Experimental apparatus

2.4.1 FO-MD hybrid module and experimental system

The hybrid module (Figure 1) was composed of three compartments: DS was recirculated in the two outer compartments and distillate was recirculated counter-currently in the middle compartment. Two FO membranes were placed on the outer faces of the module and two MD membranes were placed in the inner compartments. All membranes had effective areas of 132 cm^2. Details of the FO-MD hybrid module can be found in Ricci et al. [18].

The FO-MD module was inserted into a feed reservoir and connected to a 45 °C temperature-controlled DS reservoir. A 25 °C temperature-controlled distillate reservoir was also connected to the FO-MD module. DS and distillate reservoirs were placed on digital scales (L10001, BEL Engineering, Monza, Italy) to measure the change in weight during each run. Five diaphragm pumps (SFDP1-012-035-21, Seaflo, Fujian Liancheng County, China) were used to recirculate DS, distillate, cooling water and hot water. Flow rates were measured through three rotameters (TRP-25, Tecnofluid, Belo Horizonte, Brazil). Three temperature sensors (TD08, Tecmak, São José do Rio Preto, Brazil) were inserted in the feed, DS and distillate reservoirs.

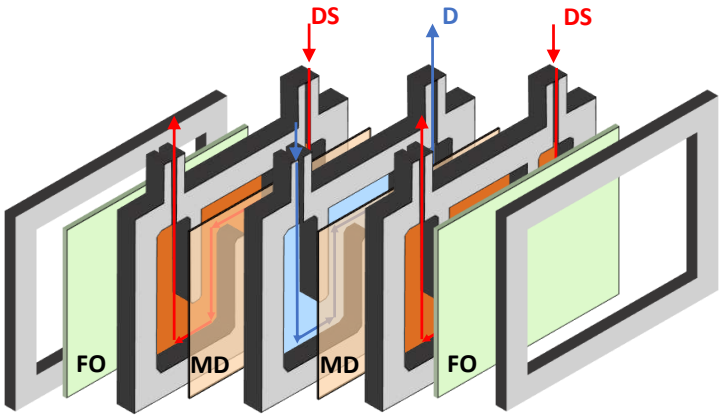

Figure 1 - Hybrid FO-MD module indicating placement of forward osmosis (FO) and distillation (MD) membranes and flow of draw solution (DS) and distillate (D).

2.4.2 Operating conditions

Prior to each test, the lab-scale FO-MD system was flushed sequentially with tap water, deionized water, nitric acid (HNO_3 5%), tap water and deionized water. Tests were started with 4.5 L of feed (deionized water spiked with 2 $\mu g.L^{-1}$ of each TrOC), 2 L of DS and 3 L of distillate (deionized water). The volume of the feed reservoir was held constant by continuously replenishing the water that crossed the FO membrane. Flow rates of DS and distillate were maintained at 75 $L.h^{-1}$ and 80 $L.h^{-1}$, respectively. Each test was carried out for 480 min during which weight of DS and distillate reservoirs were recorded at five-minute intervals and conductivities of feed, DS and distillated every 15 min. DS concentration was held constant by adding deionized water or concentrated DS to the DS reservoir. Reverse salt flux through the FO membrane (J_s) and salt flux in MD (J_{sMD}) were assessed by feed and distillate conductivity, respectively. At the end of each test, one liter each of feed, DS and distillate were collected for analysis of TrOC concentrations.

2.5 Analytical methods

Electrical conductivity was measured with a conductivity meter (HI763100, Hanna Instruments, São Paulo, Brazil). A multiple linear regression analysis in R Program [49] was used to construct the calibration curve of conductivity as function of temperature and concentration, for each salt. Salt concentrations were calculated from conductivity and temperature measurements. pH was measured with a digital pH meter (Tecnopon, mPA 210, São Paulo, Brazil).

TrOCs were quantified by liquid-chromatography (Shimadzu Prominence UFLC, Shimadzu, Kyoto, Japan) coupled with mass spectrometry (MicrOTOF-QII, Bruket Daltonics,

Bremen, Germany) (LC-MS). Before LC-MS, samples were extracted using solid phase extraction (SPE) on Strata C18 500 mg/6 mL cartridges (Prenomenex, São Paulo, Brazil). Cartridges were conditioned immediately before use with 5 mL methanol and 5 mL deionized water. The samples were forced under vacuum through the cartridge at a flow rate of approximately 10 mL.min^{-1}. After passing 1 L of sample, cartridges were washed with 10 mL deionized water and dried for 20 min [50]. The analytes were eluted with 4 mL methanol and an aliquot of 1 mL of this extract was injected in the LC-MS, operated according to the method described by Faria et al. [51].

2.6 Theoretical background and calculations

2.6.1 Water flux, salt flux and rejections

MD water flux (J_{MD}) was quantified by Eq. (3):

$$J_{MD} = \frac{m_{D,t2} - m_{D,t1}}{(t_2 - t_1) \times A_m \times \rho_D} \quad (3)$$

where $m_{D,t1}$ and $m_{D,t2}$ are the recorded masses of distillate at times t_1 and t_2, A_m is the effective membrane area and ρ_D is the density of the water at 25 °C.

FO water flux (J_{FO}) was quantified by Eq. (4):

$$J_{FO} = \frac{m_{DS,t2} - m_{DS,t1}}{(t_2 - t_1) \times A_m \times \rho_{DS}} + J_{MD} \quad (4)$$

where $m_{DS,t1}$ and $m_{DS,t2}$ are the recorded masses of DS at t_1 and t_2 and ρ_{DS} is the density of DS at 45 °C.

Dunn's test was used to compare J_{FO} and J_{MD} for the 5 salts, with $\alpha = 5\%$. Correlation between J_{FO} and D was calculated with R programming [49].

FO reverse salt flux (J_s) was determined by Eq. (5):

$$J_s = \frac{C_{F,t2} \times V_{F,t2} - C_{F,t1} \times V_{F,t1}}{(t_2 - t_1) \times A_m} \quad (5)$$

where $C_{F,t1}$ and $C_{F,t2}$ are the solute concentration of the feed and $V_{F,t1}$ and $V_{F,t2}$ are the volume of the feed solution at times t_1 and t_2.

MD salt flux of the (J_{sMD}) was quantified by Eq (6):

$$J_{sMD} = \frac{C_{D,t2} \times V_{D,t2} - C_{D,t1} \times V_{D,t1}}{(t_2 - t_1) \times A_m} \quad (6)$$

where $C_{D,t1}$ and $C_{D,t2}$ are the solute concentration of the feed and $V_{D,t1}$ and $V_{D,t2}$ are the volume of the feed solution at times t_1 and t_2.

MD salt rejection was calculated by Eq (7):

$$R = \frac{C_{DS} - C_{p,sMD}}{C_{DS}} x\ 100 \quad (7)$$

where $C_{p,sMD}$ is the final salt concentration of the MD permeate (t = 480 min) in each experiment.

TrOC rejection in FO (R_{FO}) was calculated using Eq. (8):

$$R_{FO} = \frac{C_F - C_{p,FO}}{C_F} x\ 100 \quad (8)$$

where C_F is the TrOC concentration accumulated at feed reservoir and $C_{p,FO}$ is the final TrOC concentration of the FO permeate (t = 480 min) in each experiment.

Global TrOC rejection (R_g) was calculated using Eq. (9):

$$R_g = \frac{C_F - C_{p,MD}}{C_F} x\ 100 \quad (9)$$

where $C_{p,MD}$ is the final TrOC concentration of the MD permeate (t = 480 min) in each experiment.

2.6.2 Flux equation and concentration polarization for forward osmosis

Concentration polarization in FO was calculated as proposed by McCutheon and Elimelech [52]. The observed water flux in FO ($J_{FO,obs}$) was expressed by Eq. (10):

$$J_{FO,obs} = A(\pi_{DS,i} - \pi_{F,i}) \quad (10)$$

where A is the water permeability coefficient, $\pi_{DS,i}$ is the osmotic pressure at the membrane interface and $\pi_{F,i}$ is the osmotic pressure of the feed solution at the feed-membrane interface.

Internal concentration polarization (ICP) modulus as defined by Eq. (11):

$$\frac{\pi_{DS,i}}{\pi_{DS,b}} = e^{-\frac{J_{FO,obs}}{k_{m,FO}}} \quad (11)$$

where $\pi_{DS,b}$ is the osmotic pressure of the DS and $k_{m,FO}$ is the mass transfer coefficient within the membrane support layer, calculated using Eq. (12):

$$k_{m,FO} = \frac{D_T}{S} \quad (12)$$

where S is the membrane structural parameter and D_T is the diffusion coefficient of the draw solute at the temperature (T) of the DS during the experiments, Eq. (13) [27–29].

$$D_T = D_o \frac{\mu_{T_o} T}{\mu_T T_o} \quad (13)$$

where D_o is the diffusion coefficient at the reference temperature (T_o = 25 °C), for each draw solute and μ_{To} and μ_T are the dynamic viscosity of the DS at T_o and T, respectively.

External concentration polarization (ECP) modulus was calculated by Eq. (14):

$$\frac{\pi_{F,i}}{\pi_{F,b}} = e^{\frac{J_{FO,obs}}{k_{F,FO}}} \quad (14)$$

where $\pi_{F,b}$ is the osmotic pressure of the feed solution and $k_{F,FO}$ is the mass transfer coefficient on the feed solution side of the membrane.

From Eq. (10), the model for water flux in FO was expressed by Eq. (15):

$$J_{FO,obs} = A\left[\pi_{DS,b}e^{-\frac{J_{FO,obs}}{k_{m,FO}}} - \pi_{F,b}e^{\frac{J_{FO,obs}}{k_{F,FO}}}\right] \quad (15)$$

A reference condition was established to compare the observed water flux with the highest attainable flux ($J_{FO,ref}$) without ECP, considering the ratio of permeate to feed volume (φ), according to the model (Eq. (16)) proposed by Lay et al. [53]:

$$J_{FO,ref} = A\left[\pi_{DS,b}e^{-\frac{J_{FO,ref}}{k_{m,FO}}} - \pi_{F,b}\left(\frac{1}{1-\varphi}\right)\right] \quad (16)$$

The flux efficiency factor (FEF), defined by Lay et al. [53], was used to assess the flux performance of a FO operation (Eq. (17)):

$$FEF = \frac{J_{FO,obs}}{J_{FO,ref}} \quad (17)$$

2.6.3 Polarization for membrane distillation

2.6.3.1 Temperature polarization for membrane distillation

Temperature polarization coefficient (τ) was defined by Eq. (18):

$$\tau = \frac{T_1 - T_2}{T_{DS} - T_D} \quad (18)$$

where T_1 and T_2 are the temperatures at the interface of the membrane at the feed and permeate side, respectively. T_{DS} and T_D are the temperatures measured at MD bulk feed (DS) and MD bulk permeate (distillate), respectively.

T_1 and T_2 were estimated by Eq. (19) and Eq. (20), as proposed by Srisurichan et al. [54]:

$$T_1 = \frac{\frac{k_t}{\delta}\left[T_D + \left(\frac{h_{DS}}{h_D}\right)T_{DS}\right] + h_{DS}T_{DS} - J_{MD,obs}\Delta H_v}{\frac{k_t}{\delta} + h_{DS}\left[1 + \left(\frac{k_t}{\delta\, h_D}\right)\right]} \quad (19)$$

$$T_2 = \frac{\frac{k_t}{\delta}\left[T_{DS} + \left(\frac{h_D}{h_{DS}}\right)T_D\right] + h_D T_D + J_{MD,obs}\Delta H_v}{\frac{k_t}{\delta} + h_D\left[1 + \left(\frac{k_t}{\delta\, h_{DS}}\right)\right]} \quad (20)$$

where k_t is the thermal conductivity of the membrane (90.4 $kW.m^{-1}.K^{-1}$) [18], $J_{MD,obs}$ is the observed water flux in MD, ΔH_v is the vaporization heat of water (2441.86 $kJ.kg^{-1}$ at 25 °C, [55], h_{DS} and h_D are the heat transfer coefficients in the feed and the permeate, respectively. The latter were calculated using Eq. (21).

$$h = \frac{Nu\, k_f}{L} \quad (21)$$

where k_f is the fluid thermal conductivity (DS or distillate), L is the characteristic length and Nu is the dimensionless Nusselt number, estimated by the Graetz-Lévêque empirical model for laminar flow, Eq. (22) [56,57]:

$$Nu = 1{,}86\left(Re\ Pr\frac{d_h}{L_c}\right)^{0{,}33} \quad (22)$$

where d_h is the hydraulic diameter and L_c is the channel length.

Reynolds (Re) and Prandtl (Pr) numbers were calculated using Eqs. (23) and (24):

$$Re = \frac{d_h \nu\, \rho}{\mu} \quad (23)$$

$$Pr = \frac{\mu\, c_p}{k_f} \quad (24)$$

where ν, μ, ρ and c_p are the average velocity, the dynamic viscosity, the density and the heat capacity of the fluid, respectively.

2.6.3.2 Concentration polarization for membrane distillation

Concentration polarization in MD is a result of water permeation through the membrane and draw solute accumulation at the feed solution/membrane interface. The draw solute concentration at the membrane ($C_{DS,MD}$) was calculated by Eq. (25):

$$C_{DS,MD} = C_{DS} e^{\frac{J_{MD,obs}}{k_{m,MD}}} \quad (25)$$

where C_{DS} is the MD feed (DS) concentration. $k_{m,MD}$ is the solute mass transfer coefficient within the MD membrane, that was estimated by Sherwood (Sh) and Schmidt (Sc) numbers, calculated using Eqs. (26) and (27) [57]:

$$Sh = 1{,}86\left(Re\ Sc\ \frac{d_h}{L_c}\right)^{0{,}33} \quad (26)$$

$$Sc = \frac{\mu}{\rho\ D_T} \quad (27)$$

After calculation of Sh, $k_{m,MD}$ was calculated by Eq. (28):

$$k_{m,MD} = \frac{Sh\ D_T}{d_h} \quad (28)$$

The concentration polarization coefficient (ζ) was then calculated by Eq. (29):

$$\zeta = \frac{C_{DS,MD}}{C_{DS}} \quad (29)$$

2.6.3.3 Vapor pressure polarization for membrane distillation

Vapor pressure polarization can occur at the membrane interface in MD since temperature and concentration differ from the those of the bulk solution [18]. The vapor pressure polarization coefficient (ψ) was estimated by Eq. (30):

$$\psi = \frac{P_{DS,m} - P_{D,m}}{P_{DS,b} - P_{D,b}} \quad (30)$$

where $P_{DS,m}$ and $P_{DS,b}$ are the vapor pressures at the membrane and the bulk solution on the feed side, and $P_{D,m}$ and $P_{D,b}$ are the vapor pressures at the membrane and the bulk solution on the permeate side. The vapor pressures were calculated by the change in water vapor pressure (P_w) with the water activity coefficient (a_w), that depends on temperature and concentration of the solute (Eq. (31)):

$$P = P_w\ a_w \quad (31)$$

The values of a_w, ν, μ, ρ and c_p used to calculate polarizations for each draw solute are presented in Table S2 and S3 (supplementary material), and were estimated by the models proposed by Laliberté [58,59], Kharat [60] and Wahab et al. [61] using Aspen Plus software.

2.6.4 Energy consumption for pumping

Specific energy consumption (SEC_{pump}) for distillate and DS pumping for each salt was estimated according to Eq. (32) [62]:

$$SEC_{pump} = \frac{W_{pump}}{Q_p} = \frac{n\ \Delta p\ Q_v}{Q_p} \quad (32)$$

where W_{pump} is the work done by the pump, Q_p is the permeate flow rate, n is the number of compartments (1 for distillate and 2 for DS), Δp is the pressure drop, and Q_v is the volumetric flow rate.

2.7 Application of TOPSIS for selection of the best solute for FO-MD system

The R program [49] TOPSIS package [63] was used to rank the five salts and select the best for use in hybrid FO-MD module DS. The step-by-step calculations are shown in supplementary material. The results of water and salt flux, energy consumption, costs and R_{FO} and $R_{g,}$ for each TrOC were used as decision making criteria. All 21 selection criteria and their respective weights can be found in the supplementary material (Table S5).

Weighting of TrOC rejection took into consideration anaerobic biodegradability of each compound, as previously evaluated [64]. In a hybrid anaerobic OMBR-MD system (AnOMBR-MD), the FO-MD module must be more effective in rejecting pollutants that are not biodegradable. Therefore, for biodegradable TrOC (BET), rejection received a weight of one, regardless of salinity. TrOC that are partially biodegradable and/or adsorbable onto sludge (fluconazole, loratadine and prednisone) were assigned rejection weights of 1.1. Ketoprofen rejection was given a weight of 1.2, since it is adsorbable, but biodegradable only at low salinity. Higher weight (1.5) was given to the compounds that are not biodegradable nor adsorbable (17α-ethinylestradiol and fenofibrate). If the compound was rejected by the FO membrane or by the overall process, TrOC rejection weight was multiplied by 1.5 or 3, respectively.

3 Results and discussion

3.1 Forward osmosis performance

FO water flux ($J_{FO,obs}$) declined at the beginning of each test (Figure 2a), despite $\pi_{SO,b}$ being kept constant and equal to 28 bar ($p < 0.05$). After stabilization, NaCl and $MgOAc_2$ exhibited the highest $J_{FO,obs}$ (4.8 $L.m^{-2}.h^{-1}$), followed by NaOAc (4.6 $L.m^{-2}.h^{-1}$), $MgCl_2$ (3.6 $L.m^{-2}.h^{-1}$) and EDTA-Na_2 (2.8 $L.m^{-2}.h^{-1}$) ($p < 0.05$). Differences in FO performance for each DS could be attributed to the different salt diffusion coefficients, since a small diffusion coefficient (Table 3) could result in severe internal concentration polarization (ICP). ICP is characterized by the reduction of DS concentration at the membrane active layer - support layer interface ($\pi_{DS,i}$), caused by convective water flow from the feed to the DS [21]. As a result of ICP, the effective osmotic pressure difference ($\Delta\pi_{eff}$) across the membrane is lower than in the bulk solutions, with a decrease in J_{FO}. Solutes with higher diffusion coefficients (D) are able to reconcentrate at the support layer and maintain permeate flux through the membrane. Indeed, $J_{FO,obs}$ was strongly correlated with D at the operating temperature ($R^2 = 0.9665$), as previously observed by Ansari et al. [28].

Parameters that affect FO were calculated to evaluate the process (Table 3). Although deionized water was used as feed solution, with negligible $\pi_{f,b}$, caused only by J_s, $\pi_{f,i}$ reached almost half the $\pi_{SO,b}$, due to external concentration polarization (ECP). As a result, $\Delta\pi_{eff}$ was about 4 bar for NaCl, NaOAc and $MgOAc_2$, which had higher J_{FO}, and decreased to 3 and 2.4 bar for $MgCl_2$ and EDTA-Na_2. Even though the lowest J_{FO} was observed when EDTA- Na_2 was used, its flux efficiency factor (FEF) was not the lowest, since a higher ICP, which directly impacts $J_{FO,ref}$, was expected for this salt.

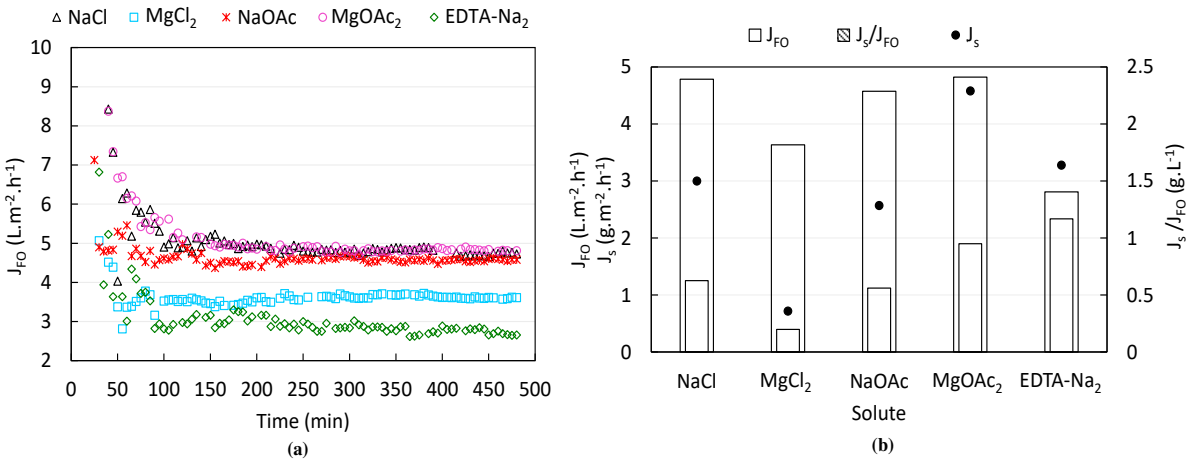

Figure 2 - (a) FO water flux and (b) average water flux (after 300 min), reverse salt flux and specific salt flux.

Table 3 - Transport parameters and osmotic pressures in FO for each DS salt evaluated

Solute	D_{45} (10^{-6} $m^2.s^{-1}$)	$k_{m,FO}$[a] (10^{-6} $m.s^{-1}$)	$k_{F,FO}$[b] (10^{-7} $m.s^{-1}$)	$\pi_{f,b}$[c] (bar)	$\pi_{f,i}$[d] (bar)	$\pi_{DS,b}$[e] (bar)	$\pi_{DS,i}$[f] (bar)[a]	$\Delta\pi_b$[g] (bar)	$\Delta\pi_{eff}$[h] (bar)	FEF[i]
NaCl	2.28	3.23	2.65	0.0962	14.4	28.0	18.5	27.8	4.1	41.0
$MgCl_2$	1.73	2.38	1.55	0.0221	15.2	28.0	18.3	28.0	3.1	36.2
NaOAc	2.30	3.25	2.25	0.0524	14.9	28.0	18.9	27.9	4.0	38.9
$MgOAc_2$	2.31	3.27	2.31	0.0432	14.4	28.0	18.6	28.0	4.1	40.7
EDTA-Na_2	0.93	1.32	1.35	0.0408	13.0	28.0	15.5	27.9	2.4	39.4

[a]Mass transfer coefficient within the FO membrane support layer; [b]Mass transfer coefficient on the feed solution side of FO membrane; [c]Osmotic pressure of the feed solution; [d]Osmotic pressure of the feed solution at the feed-membrane interface; [e]Osmotic pressure of the DS; [f]Osmotic pressure of the DS at the membrane interface; [g]Bulk osmotic pressure gradient; [h]Osmotic pressure difference across the active layer of the FO membrane; [i]Flux efficiency factor.

A serious problem in FO is J_s, which is the solute diffusion from the DS to the feed solution across the FO membrane [48,65]. As can be observed in Figure 2b, $MgCl_2$ presented lower J_s and specific salt flux (J_s/J_{FO}) values, indicating that salinity and $\pi_{f,b}$ increases in the

feed were lower, which could have a lower impact on J_{FO} in the long run and reduce costs of salt makeup. Unlike the expected, J_s values for $MgOAc_2$ and EDTA-Na_2 were 4 times higher than those previously reported for the same $\pi_{SO,b}$ ($MgOAc_2$: 1.07 $g.m^{-2}.h^{-1}$; EDTA-Na_2: 0.5 $g.m^{-2}.h^{-1}$) [28,29]. In the present study, the influence of DS temperature is clearly, since it was kept at 45 °C, due to MD, which increased FO diffusion, leading to higher J_s than would occur at ambient temperature, as was used in the literature reports.

J_s/J_{FO} values found in the literature also differ greatly from those found in the present study (NaCl: 0.57-0.59 $g.L^{-1}$; $MgCl_2$: 0.74 $g.L^{-1}$; NaOAc: 0.25-0.3 $g.L^{-1}$; $MgOAc_2$: 0.13-0.2 $g.L^{-1}$; EDTA-Na_2: 0.2 $g.L^{-1}$) [27–29]. Besides temperature, that may have increased J_{FO}, since it reduced water viscosity, the FO membrane used (CTA-FTS) has a larger structure parameter (S = 707 µm) than membranes in the articles cited (CTA, Hydration Technology Innovations, S = 427 µm). Furthermore, ICP, which reduces J_{FO}, is more severe in the hybrid submerged FO-MD module than in an external FO module [18].

3.2 Membrane distillation performance

Permeate flux through the distillation membrane (J_{MD}) sharply decreased at the beginning of the tests (Figure 3), with the highest to lowest values after stabilization as follows: NaOAc (4.0 $L.m^{-2}.h^{-1}$) > NaCl (3.8 $L.m^{-2}.h^{-1}$) > $MgCl_2$ (3.3 $L.m^{-2}.h^{-1}$) > $MgOAc_2$ (3.1 $L.m^{-2}.h^{-1}$) ($p < 0.05$). Flux did not stabilize even after 480 min when EDTA-Na_2 was used and the final $J_{MD,obs}$ observed was 3.0 $L.m^{-2}.h^{-1}$.

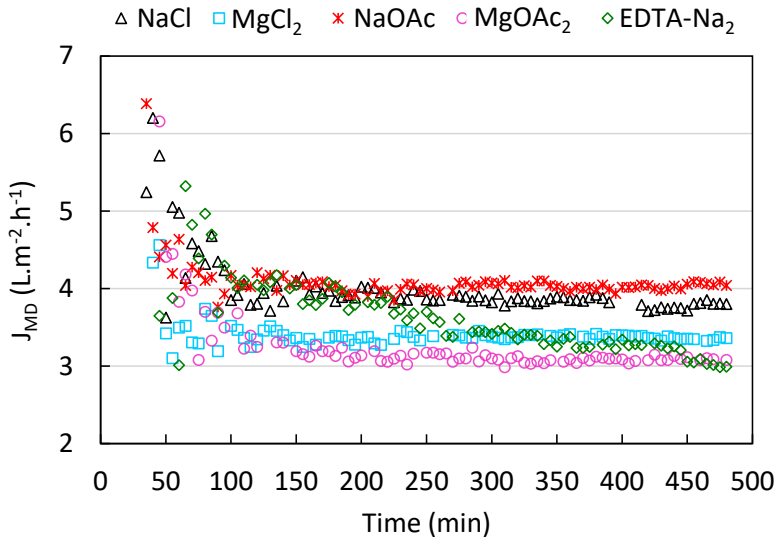

Figure 3 - MD water flux using different draw solution solutes.

According to Ramezanianpour and Sivakumar [66], J_{MD} reduction depends not only on ΔT and circulation velocity but also on feed concentration, viscosity and density. The authors justify that with the increase in these three variables, rapid blockage of membrane pores can occur, leading to decrease in J_{MD}, but another important factor is the decrease in water activity that leads to decreased vapor pressure. The highest ΔT during the tests was found for $MgOAc_2$, however, contrary to what was expected, this salt did not have the highest J_{MD}, possibly because of its higher DS concentration (Table 1).

Sharp temperature polarization occurred during the tests (Table 4), reducing the MD driving force, with ΔT on the membrane surface varying from 1.1 °C for NaCl up to 2.5 °C for $MgOAc_2$, that had the highest temperature polarization coefficient (τ). In MD process, water permeation through the membrane results in draw solute accumulations at the feed solution/membrane interface, a phenomenon called concentration polarization [18]. All solute concentrations increased on the feed side of the distillation membrane, with the highest for $MgOAc_2$, in agreement with the lowest J_{MD} found for this salt. The highest concentration polarization (ζ) was observed for EDTA-Na_2, with $C_{DS,MD}$ of 117.39 $g.L^{-1}$. EDTA-Na_2 solubility at 34.4 °C calculated by interpolation of data from Perry [67] is 116.16 $g.L^{-1}$, suggesting that this salt may have precipitated on the distillation membrane during operation, leading to pore blockage and continuous reduction of J_{MD}. Therefore, salt solubility is an important factor for MD process. Although $MgOAc_2$ had the highest vapor pressure polarization coefficient (ψ), its bulk solution concentration and membrane vapor pressures were among the lowest, because the salt´s high concentration that besides causing pore blockage also reduced vapor pressure and consequently the MD driving force.

Despite the differences in J_{MD}, NaCl and $MgCl_2$ were the only solutes completely rejected throughout the tests (Figure 4), favoring MD regeneration of DS using these salts. Some salt flux (below 0.68 $g.m^{-2}.h^{-1}$) and increase in distillate salinity were observed for NaOAc, $MgOAc_2$ and EDTA-Na_2, although salt rejection was greater than 99.7%. Siddique et al. [15] reported sodium and magnesium acetate salt rejection during MD greater than 98%, indicating some salt flux through the distillation membrane. Since these two acetate salts are ionized to form acetate anion (CH_3COO^-) and Mg^{2+} or Na^+, passage of the anion to the distillate can occur, considering that vapor pressure difference between the DS and the distillate for acetic acid is 3940 Pa [68]. A higher increase in distillate salt concentration was found for $MgOAc_2$, with double $C_{DS,bulk}$ compared to NaOAc.

For EDTA-Na_2, passage of the salt through the membrane micropores, also reported by Nguyen et al. [40], may have resulted from salt precipitation on the distillation membrane surface. This is a drawback to use of EDTA-Na_2 as DS, since higher concentrations are necessary to achieve high flux, but these favor precipitation on both the distillation and FO membranes, since the FO feed may be at a lower temperature than the DS.

In the long run, the three organic solutes may increase operating costs for DS makeup and worsen distillate quality by increasing their dissolved solids and organic carbon contents, which will not occur using NaCl and $MgCl_2$.

Table 4 - Polarization in the MD process for different FO draw solution solutes in an integrated FO-MD module

Solute	T_{DS}[a] (°C)	T_D[b] (°C)	T_1[c] (°C)	T_2[d] (°C)	τ[e]	$C_{DS,MD}$[f] (g.L^{-1})	ζ[g]	P_{DS}[h] (Pa)	$P_{DS,m}$[i] (Pa)	ψ[j]
NaCl	44.6	25.7	35.5	34.4	0.060	40.95	1.22	9184	5665	0.040
$MgCl_2$	45.1	26.2	36.2	34.7	0.082	42.27	1.24	9490	5930	0.069
NaOAc	44.6	24.9	35.4	34.1	0.062	63.78	1.24	9154	5597	0.051
$MgOAc_2$	45.0	23.6	35.6	33.0	0.119	131.54	1.17	8852	5359	0.085
EDTA-2Na	44.5	24.4	34.4	32.6	0.091	117.39	1.33	8313	4808	0.035

[a]Temperature of bulk DS; [b]Temperature of bulk distillate; [c]Temperature at MD feed surface; [d]Temperature at MD permeate surface; [e]Temperature polarization coefficient in MD; [f]DS concentration at MD surface; [g]Concentration polarization coefficient in MD; [h]Vapor pressure in bulk DS; [i]Vapor pressure at MD feed surface; [j]Vapor pressure polarization coefficient in MD.

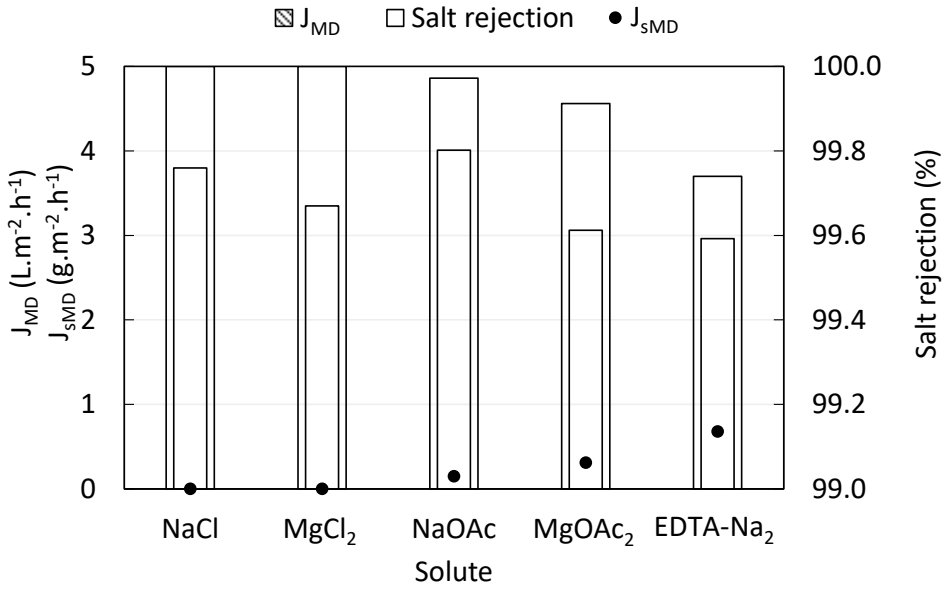

Figure 4 - Average MD water flux (after 300 min), salt flux and salt rejection.
(For EDTA-Na_2, J_{MD} did not stabilize and the value presented is for the final flux observed)

3.3 TrOC rejection

TrOC rejection by the FO membrane (Figure 5a) for the different DS was related to J_s. Salt diffusion from the DS to the feed caused by the increase in ionic force could lead to a decrease in hydrogen bonds on the FO membrane surface, which would increase the average pore size and decrease the rejection of dissolved compounds [23,69]. In fact, when $MgCl_2$ and NaOAc were used, lowest J_s was observed and FO membrane presented the highest TrOC rejection. Solutes with higher J_s exhibited lower R_{FO}, with the lowest rejection for $MgOAc_2$ (J_s = 4.58 $g.m^{-2}.h^{-1}$), followed by EDTA-Na_2 (J_s = 3.28 $g.m^{-2}.h^{-1}$) and NaCl (J_s = 3 $g.m^{-2}.h^{-1}$). Besides Js, it seems that FEF also influences TrOC rejection by FO membrane, since it represents flux performance in FO operation, compared to a reference condition [53]. $MgCl_2$ and NaOAc had the lowest values of FEF, indicating that higher permeate flux, for a given recovery (φ) can facilitate the transport of micropollutants through the FO membrane, but it still needs to be investigated.

Besides the DS salt, the principal rejection mechanisms in FO are size exclusion and electrostatic interactions. High R_{FO} was observed for 17α-ethynylestradiol, with undetectable DS concentrations for all salts because of this compound´s hydrophobicity (log K_{OW} = 3.9) and non-interaction with the FO membrane [70]. R_{FO} between 68 and 92% was found for ketoprofen, the TrOC with the lowest molar mass. For betamethasone, fluconazole and prednisone, rejections of 62% were observed, probably because of these compounds' hydrophilicity (log K_{OW} = 1.68, 0.56 e 1.66, respectively), that favored interaction with the FO membrane and consequently passage to the DS.

The isoelectric point for the studied FO membrane is 4, which means that above this pH, membrane has a negative surface charge [66]. Given the pH of the feed solution, DS and distillate (Table S4), the highest R_{FO} was expected for ketoprofen, the only negatively charged TrOC. However, in this study electrostatic interactions were not a predominant factor in FO TrOC rejection, as likewise found by Sauchelli et al. [24], since ketoprofen had the lowest R_{FO}.

Distillate concentrations were below detection limits for almost all TrOCs, since they are non-volatile compounds (Figure 5b). Prednisone was detected when NaOAc was used as DS, but R_g (98,14%) was still high. Ketoprofen´s hydrophobicity (log K_{OW} = 3.6) may have contributed to its interaction with the distillation membrane and passage to the distillate, despite its negligible volatility (pK_H = 10.67) [71,72]. On the other hand, ketoprofen R_g was higher with EDTA-Na_2 as DS, which may have been a result of salt precipitation and distillation membrane pore blockage as discussed in item 3.2.

It should be mentioned that the increase in fouling during the operation of an OMBR would contribute to greater electrostatic repulsion on the FO membrane that would increase TrOC rejection [18,73]. Under this scenario, the concentration of the compounds, especially ketoprofen, will be lower in the DS, and thus their passage to the distillate will also be lower.

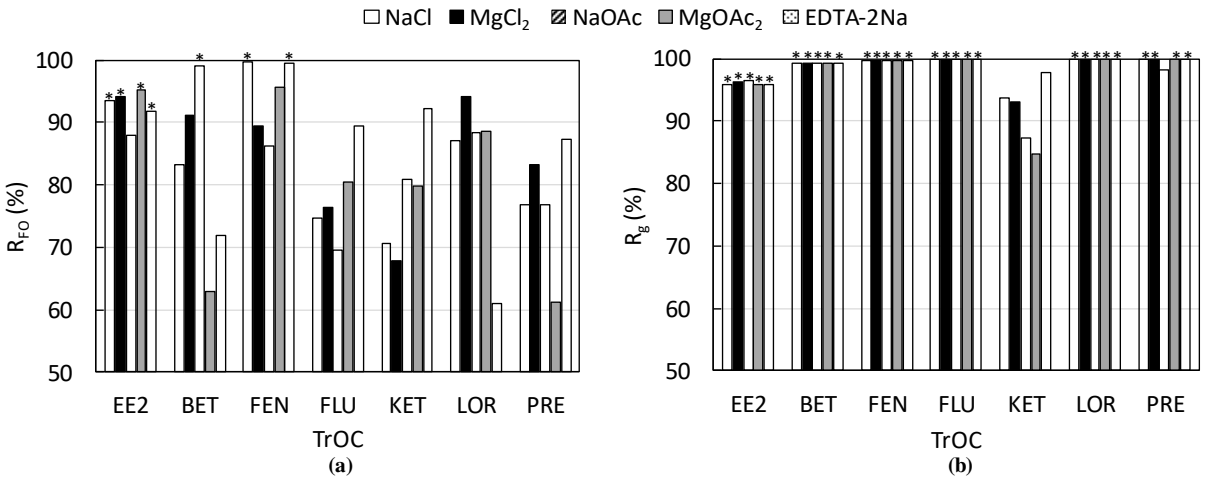

Figure 5 - (a) TrOC rejection by FO membrane; (b) TrOC global rejection in the submerged hybrid FO-MD module. * TrOC concentration was below detection limit.

3.4 Costs and energy consumption

DS costs and energy consumption are important in selecting the best solute for DS since they affect investment and operating costs. Initial investment costs to prepare DS solutions at fixed $\pi_{SO,b}$ varied from 0.11 to 4.20 U$.L^{-1} (Table 5), with NaCl's the lowest. Besides the higher unit cost of $MgOAc_2$, this solute was required at the highest concentration for the given $\pi_{SO,b}$, resulting in higher overall cost. Costs of DS makeup to maintain $\pi_{SO,b}$ varied from 2.08 to 40.41 U$.m^{-3} of permeate (Table 4). Again, the highest value was found for $MgOAc_2$, since, differently from the study by Bowden et al. [29], J_s was very high and the salt was also lost to the distillate. $MgCl_2$ presented costs competitive with NaCl since it had the lowest J_s and intermediate unit cost.

EDTA-Na_2 demanded the highest energy consumption for pumping solutions, as a result of the low FO and MD permeate fluxes that reduced SEC_{pump}. $MgCl_2$ also consumed more energy than the other three salts, with higher consumption for DS pumping, since its J_{FO} was low.

Table 5 - DS preparation and makeup costs and specific energy consumption for pumping

Salt	Unit cost (U$.kg^{-1})	DS cost (U$.L^{-1})[a]	DS makeup cost (U$.m^{-3})[b]	SEC_{pump} (kW.m^{-3}.d^{-1})[c]
NaCl	3.26	0.11	2.08	0.155
$MgCl_2$	14.47	0.49	2.89	0.190
NaOAc	12.17	0.63	7.58	0.155
$MgOAc_2$	37.50	4.20	40.41	0.175
EDTA-Na_2	15.80	1.39	22.85	0.221

[a]Cost to produce 1 L of DS at the concentration for osmotic pressure equal to 28 bar; [b]Cost per m^3 of permeate to make up loss of solute through J_s and J_{sMD}; [c]Specific energy consumption for pumping DS and distillate in the hybrid FO-MD module.

3.5 Selection of the best DS salt for the FO-MD module

According to the multicriteria analysis by TOPSIS, $MgCl_2$ is the salt with the shortest Euclidean distance to the positive ideal solution (D+) and the highest Euclidean distance to the negative ideal solution (D-) (Table 6). Therefore, after calculation of similarity with the positive ideal solution, $MgCl_2$, was the best solute, for operation of the hybrid submerged FO-MD module in OMBR-MD. Radar plots, comparing $MgCl_2$ with the positive and the negative ideal solutions, are presented in Figure 6. The rank was followed by NaCl, NaOAc, EDTA-Na_2 and $MgOAc_2$.

As previously discussed, despite low J_{FO}, operation with $MgCl_2$ had lower J_s and J_s/J_{FO}, with replenishment costs comparable to NaCl, which resulted in it being the farthest from the negative ideal solution and closest to the positive ideal solution. In addition, high TrOC rejections were obtained in both FO and the hybrid FO-MD module using $MgCl_2$. Therefore, $MgCl_2$ was selected as the best solute for DS in treatment of effluents containing micropollutants in an OMBR-MD system.

Table 6 - TOPSIS Euclidean distances and ranking of the 5 alternatives draw solution salts

	NaCl	$MgCl_2$	NaOAc	$MgOAc_2$	EDTA-Na_2
[a]D^+	1.043	0.642	1.138	3.732	3.377
[b]D^-	4.216	4.328	3.590	1.658	1.833
[c]R^+	0.802	0.871	0.759	0.308	0.352
Rank	2	1	3	5	4

[a]D^+: Euclidean distance to the positive ideal solution; [b]D^-: Euclidean distance to the negative ideal solution; [c]R^+: Similarity to ideal solution.

Of the 14 inorganic solutions tested by Achilli et al. [27], $MgCl_2$ was also considered one of the best because it presented lower inorganic fouling potential. Ansari et al. [28] and

Bowden et al. [29] concluded that organic solutes (NaOAc, $MgOAc_2$ and sodium propionate) are more appropriate for OMBR compared to NaCl and $MgCl_2$, despite their higher DS reconcentration costs by reverse osmosis. However, these authors used an external FO module at 25 °C, while in the present study, under operation at 45 °C, the worst results were obtained for $MgOAc_2$, that exhibited high J_s and J_{sMD} and the lowest TrOC rejection in FO, as well being the salt with the highest unit cost.

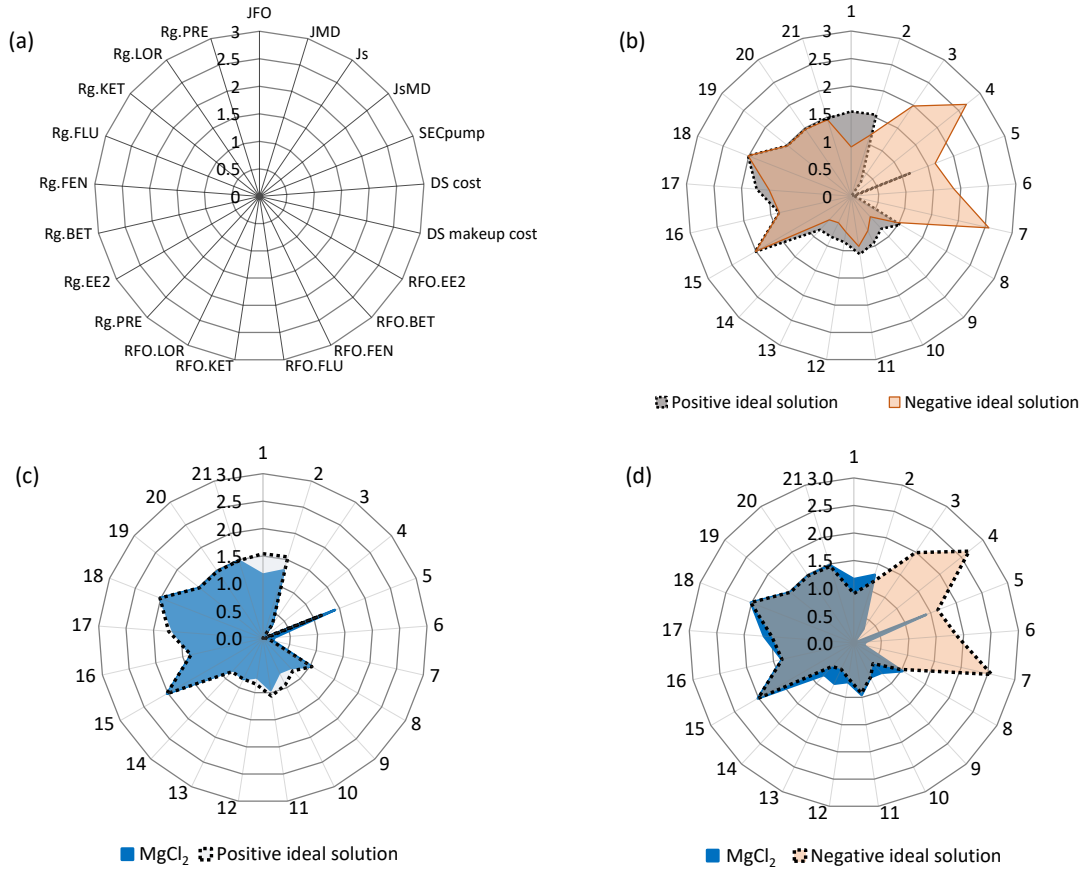

Figure 6 - Radar plots with the normalized weighs for: (a) criteria; (b) positive ideal solution and negative ideal solution; (c) $MgCl_2$ and the positive ideal solution; and (d) $MgCl_2$ and the negative ideal solution.

4 Conclusions

$MgCl_2$ presented the lowest J_{FO} and J_s, with reduction in specific system salt flux, as opposed to NaCl, NaOAc and $MgOAc_2$, which had high J_{FO} and very high J_s, that could be harmful to microbial activity in a biological reactor. $MgOAc_2$ was prejudicial to J_{MD} probably because of the high concentration needed to maintain draw solution osmotic pressure. Only the

inorganic salts were completely rejected by the distillation membrane, producing better quality distillate and reducing the need for draw solution replenishment EDTA-Na_2 presented low permeate flux and high salt flux in both forward osmosis and membrane distillation.

TrOC rejection in FO was highest when $MgCl_2$ and NaOAc were used as draw solution while use of $MgAOc_2$ resulted in the lowest rejection because of its elevated J_s. Size exclusion had more impact in FO rejection than electrostatic interactions. Regardless of the draw solutes, the integrated FO-MD module could effectively remove 6 of the 7 TrOC, and Ketoprofen was the only pharmaceutical drug detected in the distillate.

$MgCl_2$ was selected as the best salt for the draw solution in an integrated osmotic membrane bioreactor-membrane distillation system and could be used to mitigate salinity build-up in the mixed liquor, followed in order of rank by NaCl, NaOAc, EDTA-Na_2 and $MgOAc_2$ using the multicriteria decision making analysis TOPSIS.

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References

[1] S.K. Maeng, B.G. Choi, K.T. Lee, K.G. Song, Influences of solid retention time, nitrification and microbial activity on the attenuation of pharmaceuticals and estrogens in membrane bioreactors, Water Research. 47 (2013) 3151–3162. https://doi.org/10.1016/j.watres.2013.03.014.

[2] F. Meng, S.-R. Chae, A. Drews, M. Kraume, H.-S. Shin, F. Yang, Recent advances in membrane bioreactors (MBRs): Membrane fouling and membrane material, Water Research. 43 (2009) 1489–1512. https://doi.org/10.1016/j.watres.2008.12.044.

[3] Y. Li, B. Zhang, G. Li, W. Luo, Osmotic Membrane Bioreactor and Its Hybrid Systems for Wastewater Reuse and Resource Recovery: Advances, Challenges, and Future Directions, Current Pollution Reports. 4 (2018) 23–34. https://doi.org/10.1007/s40726-018-0080-1.

[4] G. Qiu, S. Zhang, D.S. Srinivasa Raghavan, S. Das, Y.-P. Ting, The potential of hybrid forward osmosis membrane bioreactor (FOMBR) processes in achieving high throughput treatment of municipal wastewater with enhanced phosphorus recovery, Water Research. 105 (2016) 370–382. https://doi.org/10.1016/j.watres.2016.09.017.

[5] M. Xie, L.D. Nghiem, W.E. Price, M. Elimelech, Comparison of the removal of hydrophobic trace organic contaminants by forward osmosis and reverse osmosis, Water Research. 46 (2012) 2683–2692. https://doi.org/10.1016/j.watres.2012.02.023.

[6] A. Alturki, J. McDonald, S.J. Khan, F.I. Hai, W.E. Price, L.D. Nghiem, Performance of a novel osmotic membrane bioreactor (OMBR) system: Flux stability and removal of trace organics, Bioresource Technology. 113 (2012) 201–206. https://doi.org/10.1016/j.biortech.2012.01.082.

[7] W. Luo, H.V. Phan, G. Li, F.I. Hai, W.E. Price, M. Elimelech, L.D. Nghiem, An Osmotic Membrane Bioreactor–Membrane Distillation System for Simultaneous Wastewater Reuse and Seawater Desalination: Performance and Implications, Environmental Science & Technology. 51 (2017) 14311–14320. https://doi.org/10.1021/acs.est.7b02567.

[8] T. Cath, A. Childress, M. Elimelech, Forward osmosis: Principles, applications, and recent developments, Journal of Membrane Science. 281 (2006) 70–87. https://doi.org/10.1016/j.memsci.2006.05.048.

[9] X. Wang, V.W.C. Chang, C.Y. Tang, Osmotic membrane bioreactor (OMBR) technology for wastewater treatment and reclamation: Advances, challenges, and prospects for the future, Journal of Membrane Science. 504 (2016) 113–132. https://doi.org/10.1016/j.memsci.2016.01.010.

[10] S. Zhao, L. Zou, C.Y. Tang, D. Mulcahy, Recent developments in forward osmosis: Opportunities and challenges, Journal of Membrane Science. 396 (2012) 1–21. https://doi.org/10.1016/j.memsci.2011.12.023.

[11] H. Luo, Q. Wang, T.C. Zhang, T. Tao, A. Zhou, L. Chen, X. Bie, A review on the recovery methods of draw solutes in forward osmosis, Journal of Water Process Engineering. 4 (2014) 212–223. https://doi.org/10.1016/j.jwpe.2014.10.006.

[12] T. Husnain, Y. Liu, R. Riffat, B. Mi, Integration of forward osmosis and membrane distillation for sustainable wastewater reuse, Separation and Purification Technology. 156 (2015) 424–431. https://doi.org/10.1016/j.seppur.2015.10.031.

[13] Y. Kim, S. Li, L. Francis, Z. Li, R.V. Linares, A.S. Alsaadi, M. Abu-Ghdaib, H.S. Son, G. Amy, N. Ghaffour, Osmotically and Thermally Isolated Forward Osmosis–Membrane Distillation (FO–MD) Integrated Module, Environmental Science & Technology. (2019). https://doi.org/10.1021/acs.est.8b05587.

[14] N.C. Nguyen, H.T. Nguyen, S.-S. Chen, H.H. Ngo, W. Guo, W.H. Chan, S.S. Ray, C.-W. Li, H.-T. Hsu, A novel osmosis membrane bioreactor-membrane distillation hybrid system for wastewater treatment and reuse, Bioresource Technology. 209 (2016) 8–15. https://doi.org/10.1016/j.biortech.2016.02.102.

[15] M.S. Siddique, S.J. Khan, M.A. Shahzad, M.S. Nawaz, N.P. Hankins, Insight into the effect of organic and inorganic draw solutes on the flux stability and sludge characteristics in

the osmotic membrane bioreactor, Bioresource Technology. 249 (2018) 758–766. https://doi.org/10.1016/j.biortech.2017.10.064.

[16] M. Xie, L.D. Nghiem, W.E. Price, M. Elimelech, A Forward Osmosis–Membrane Distillation Hybrid Process for Direct Sewer Mining: System Performance and Limitations, Environmental Science & Technology. 47 (2013) 13486–13493. https://doi.org/10.1021/es404056e.

[17] L. Zohrabian, N.P. Hankins, R.W. Field, Hybrid forward osmosis-membrane distillation system: Demonstration of technical feasibility, Journal of Water Process Engineering. 33 (2020) 101042. https://doi.org/10.1016/j.jwpe.2019.101042.

[18] B.C. Ricci, B. Skibinski, K. Koch, C. Mancel, C. Celestino, I. Cunha, M.R. Silva, C.B. Alvim, C. Faria, L. Andrade, L.C. Lange, M.C.S. Amaral, Critical performance assessment of a submerged hybrid forward osmosis - membrane distillation system, Desalination. (2019).

[19] Q. Ge, M. Ling, T.-S. Chung, Draw solutions for forward osmosis processes: Developments, challenges, and prospects for the future, Journal of Membrane Science. 442 (2013) 225–237. https://doi.org/10.1016/j.memsci.2013.03.046.

[20] N. Ghaffour, S. Soukane, J.-G. Lee, Y. Kim, A. Alpatova, Membrane distillation hybrids for water production and energy efficiency enhancement: A critical review, Applied Energy. 254 (2019) 113698. https://doi.org/10.1016/j.apenergy.2019.113698.

[21] D.J. Johnson, W.A. Suwaileh, A.W. Mohammed, N. Hilal, Osmotic's potential: An overview of draw solutes for forward osmosis, Desalination. 434 (2018) 100–120. https://doi.org/10.1016/j.desal.2017.09.017.

[22] N.C. Nguyen, H.C. Duong, H.T. Nguyen, S.-S. Chen, H.Q. Le, H.H. Ngo, W. Guo, C.C. Duong, N.C. Le, X.T. Bui, Forward osmosis–membrane distillation hybrid system for desalination using mixed trivalent draw solution, Journal of Membrane Science. 603 (2020) 118029. https://doi.org/10.1016/j.memsci.2020.118029.

[23] Y. Kim, S. Li, L. Chekli, Y.C. Woo, C.-H. Wei, S. Phuntsho, N. Ghaffour, T. Leiknes, H.K. Shon, Assessing the removal of organic micro-pollutants from anaerobic membrane bioreactor effluent by fertilizer-drawn forward osmosis, Journal of Membrane Science. 533 (2017) 84–95. https://doi.org/10.1016/j.memsci.2017.03.027.

[24] M. Sauchelli, G. Pellegrino, A. D'Haese, I. Rodríguez-Roda, W. Gernjak, Transport of trace organic compounds through novel forward osmosis membranes: Role of membrane properties and the draw solution, Water Research. 141 (2018) 65–73. https://doi.org/10.1016/j.watres.2018.05.003.

[25] L. Zheng, W.E. Price, J. McDonald, S.J. Khan, T. Fujioka, L.D. Nghiem, New insights into the relationship between draw solution chemistry and trace organic rejection by forward osmosis, Journal of Membrane Science. 587 (2019) 117184. https://doi.org/10.1016/j.memsci.2019.117184.

[26] M.A. Shahzad, S.J. Khan, M.S. Siddique, Draw solution recovery using direct contact membrane distillation (DCMD) from osmotic membrane bioreactor (Os-MBR), Journal of Water Process Engineering. (2017). https://doi.org/10.1016/j.jwpe.2017.08.022.

[27] A. Achilli, T.Y. Cath, A.E. Childress, Selection of inorganic-based draw solutions for forward osmosis applications, Journal of Membrane Science. 364 (2010) 233–241. https://doi.org/10.1016/j.memsci.2010.08.010.

[28] A.J. Ansari, F.I. Hai, W. Guo, H.H. Ngo, W.E. Price, L.D. Nghiem, Selection of forward osmosis draw solutes for subsequent integration with anaerobic treatment to facilitate resource recovery from wastewater, Bioresource Technology. 191 (2015) 30–36. https://doi.org/10.1016/j.biortech.2015.04.119.

[29] K.S. Bowden, A. Achilli, A.E. Childress, Organic ionic salt draw solutions for osmotic membrane bioreactors, Bioresource Technology. 122 (2012) 207–216. https://doi.org/10.1016/j.biortech.2012.06.026.

[30] W. Luo, F.I. Hai, W.E. Price, W. Guo, H.H. Ngo, K. Yamamoto, L.D. Nghiem, Phosphorus and water recovery by a novel osmotic membrane bioreactor–reverse osmosis system, Bioresource Technology. 200 (2016) 297–304. https://doi.org/10.1016/j.biortech.2015.10.029.

[31] C.-L. Hwang, K. Yoon, Multiple Attribute Decision Making: Methods and Applications A State-of-the-Art Survey, Springer-Verlag, Berlin Heidelberg, 1981. https://doi.org/10.1007/978-3-642-48318-9.

[32] P.P. Kalbar, S. Karmakar, S.R. Asolekar, Selection of an appropriate wastewater treatment technology: A scenario-based multiple-attribute decision-making approach, Journal of Environmental Management. 113 (2012) 158–169. https://doi.org/10.1016/j.jenvman.2012.08.025.

[33] A. Kluczek, B. Gladysz, Analytical Hierarchy Process/Technique for Order Preference by Similarity to Ideal Solution-based approach to the generation of environmental improvement options for painting process e Results from an industrial case study, Journal of Cleaner Production. 101 (2015) 360–367. https://doi.org/10.1016/j.jclepro.2015.03.079.

[34] S. Nawaz, Y. Ali, Factors Affecting the Performance of Water Treatment Plants in Pakistan, Water Conserv Sci Eng. 3 (2018) 191–203. https://doi.org/10.1007/s41101-018-0051-9.

[35] J. Qu, X. Meng, H. Yu, H. You, A triangular fuzzy TOPSIS-based approach for the application of water technologies in different emergency water supply scenarios, Environ Sci Pollut Res. 23 (2016) 17277–17286. https://doi.org/10.1007/s11356-016-6911-y.

[36] A. Afshar, M.A. Mariño, M. Saadatpour, A. Afshar, Fuzzy TOPSIS Multi-Criteria Decision Analysis Applied to Karun Reservoirs System, Water Resour Manage. 25 (2011) 545–563. https://doi.org/10.1007/s11269-010-9713-x.

[37] M.S. Islam, R. Sadiq, M.J. Rodriguez, H. Najjaran, A. Francisque, M. Hoorfar, Evaluating Water Quality Failure Potential in Water Distribution Systems: A Fuzzy-TOPSIS-OWA-based Methodology, Water Resour Manage. 27 (2013) 2195–2216. https://doi.org/10.1007/s11269-013-0283-6.

[38] C. Estay-Ossandon, A. Mena-Nieto, N. Harsch, Using a fuzzy TOPSIS-based scenario analysis to improve municipal solid waste planning and forecasting: A case study of Canary

archipelago (1999–2030), Journal of Cleaner Production. 176 (2018) 1198–1212. https://doi.org/10.1016/j.jclepro.2017.10.324.

[39] L. Chekli, S. Phuntsho, J.E. Kim, J. Kim, J.Y. Choi, J.-S. Choi, S. Kim, J.H. Kim, S. Hong, J. Sohn, H.K. Shon, A comprehensive review of hybrid forward osmosis systems: Performance, applications and future prospects, Journal of Membrane Science. 497 (2016) 430–449. https://doi.org/10.1016/j.memsci.2015.09.041.

[40] N.C. Nguyen, S.-S. Chen, S.-T. Ho, H.T. Nguyen, S.S. Ray, N.T. Nguyen, H.-T. Hsu, N.C. Le, T.T. Tran, Optimising the recovery of EDTA-2Na draw solution in forward osmosis through direct contact membrane distillation, Separation and Purification Technology. 198 (2018) 108–112. https://doi.org/10.1016/j.seppur.2017.02.001.

[41] H. Gong, D.D. Anastasio, K. Wang, J.R. McCutcheon, Finding better draw solutes for osmotic heat engines: Understanding transport of ions during pressure retarded osmosis, Desalination. 421 (2017) 32–39. https://doi.org/10.1016/j.desal.2017.03.030.

[42] S.F. de Aquino, E.M.F. Brandt, C.A. de L. Chernicharo, Remoção de fármacos e desreguladores endócrinos em estações de tratamento de esgoto: revisão da literatura, Engenharia Sanitária e Ambiental. 18 (2013) 187–204. https://doi.org/10.1590/S1413-41522013000300002.

[43] C.F. Couto, L.C. Lange, M.C.S. Amaral, A critical review on membrane separation processes applied to remove pharmaceutically active compounds from water and wastewater, Journal of Water Process Engineering. 26 (2018) 156–175. https://doi.org/10.1016/j.jwpe.2018.10.010.

[44] A.F.S. Foureaux, E.O. Reis, Y. Lebron, V. Moreira, L.V. Santos, M.S. Amaral, L.C. Lange, Rejection of pharmaceutical compounds from surface water by nanofiltration and reverse osmosis, Separation and Purification Technology. 212 (2019) 171–179. https://doi.org/10.1016/j.seppur.2018.11.018.

[45] E.O. Reis, A.F.S. Foureaux, J.S. Rodrigues, V.R. Moreira, Y.A.R. Lebron, L.V.S. Santos, M.C.S. Amaral, L.C. Lange, Occurrence, removal and seasonal variation of pharmaceuticals in Brasilian drinking water treatment plants, Environmental Pollution. 250 (2019) 773–781. https://doi.org/10.1016/j.envpol.2019.04.102.

[46] H.T. Madsen, S.S. Nissen, J. Muff, E.G. Søgaard, Pressure retarded osmosis from hypersaline solutions: Investigating commercial FO membranes at high pressures, Desalination. 420 (2017) 183–190. https://doi.org/10.1016/j.desal.2017.06.028.

[47] B.C. Ricci, C.D. Ferreira, A.O. Aguiar, M.C.S. Amaral, Integration of nanofiltration and reverse osmosis for metal separation and sulfuric acid recovery from gold mining effluent, Separation and Purification Technology. 154 (2015) 11–21. https://doi.org/10.1016/j.seppur.2015.08.040.

[48] C.Y. Tang, Q. She, W.C.L. Lay, R. Wang, A.G. Fane, Coupled effects of internal concentration polarization and fouling on flux behavior of forward osmosis membranes during humic acid filtration, Journal of Membrane Science. 354 (2010) 123–133. https://doi.org/10.1016/j.memsci.2010.02.059.

[49] R Core Team, R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing. Versão 3.2.1, (2015). https://www.r-project.org/ (accessed November 9, 2017).

[50] M. Gros, S. Rodríguez-Mozaz, D. Barceló, Rapid analysis of multiclass antibiotic residues and some of their metabolites in hospital, urban wastewater and river water by ultra-high-performance liquid chromatography coupled to quadrupole-linear ion trap tandem mass spectrometry, Journal of Chromatography A. 1292 (2013) 173–188. https://doi.org/10.1016/j.chroma.2012.12.072.

[51] C.V. Faria, B.C. Ricci, A.F.R. Silva, M.C.S. Amaral, F.V. Fonseca, Removal of micropollutants in domestic wastewater by expanded granular sludge bed membrane bioreactor, Process Safety and Environmental Protection. 136 (2020) 223–233. https://doi.org/10.1016/j.psep.2020.01.033.

[52] J.R. McCutcheon, M. Elimelech, Influence of concentrative and dilutive internal concentration polarization on flux behavior in forward osmosis, Journal of Membrane Science. 284 (2006) 237–247. https://doi.org/10.1016/j.memsci.2006.07.049.

[53] W.C.L. Lay, J. Zhang, C. Tang, R. Wang, Y. Liu, A.G. Fane, Factors affecting flux performance of forward osmosis systems, Journal of Membrane Science. 394–395 (2012) 151–168. https://doi.org/10.1016/j.memsci.2011.12.035.

[54] S. Srisurichan, R. Jiraratananon, A. Fane, Mass transfer mechanisms and transport resistances in direct contact membrane distillation process, Journal of Membrane Science. 277 (2006) 186–194. https://doi.org/10.1016/j.memsci.2005.10.028.

[55] C.O. Popiel, J. Wojtkowiak, Simple Formulas for Thermophysical Properties of Liquid Water for Heat Transfer Calculations (from 0°C to 150°C), Heat Transfer Engineering. 19 (1998) 87–101. https://doi.org/10.1080/01457639808939929.

[56] L. Martínez, J.M. Rodríguez-Maroto, On transport resistances in direct contact membrane distillation, Journal of Membrane Science. 295 (2007) 28–39. https://doi.org/10.1016/j.memsci.2007.02.029.

[57] L. Martínez-Díez, M.I. Vázquez-González, Temperature and concentration polarization in membrane distillation of aqueous salt solutions, Journal of Membrane Science. 156 (1999) 265–273. https://doi.org/10.1016/S0376-7388(98)00349-4.

[58] M. Laliberté, Model for Calculating the Viscosity of Aqueous Solutions, J. Chem. Eng. Data. 52 (2007) 321–335. https://doi.org/10.1021/je0604075.

[59] M. Laliberté, A Model for Calculating the Heat Capacity of Aqueous Solutions, with Updated Density and Viscosity Data, J. Chem. Eng. Data. 54 (2009) 1725–1760. https://doi.org/10.1021/je8008123.

[60] S.J. Kharat, Density, viscosity and ultrasonic velocity studies of aqueous solutions of sodium acetate at different temperatures, Journal of Molecular Liquids. 140 (2008) 10–14. https://doi.org/10.1016/j.molliq.2007.12.006.

[61] A. Wahab, S. Mahiuddin, G. Hefter, W. Kunz, Densities, Ultrasonic Velocities, Viscosities, and Electrical Conductivities of Aqueous Solutions of $Mg(OAc)_2$ and $Mg(NO_3)_2$, J. Chem. Eng. Data. 51 (2006) 1609–1616. https://doi.org/10.1021/je060107n.

[62] A. Zhu, P.D. Christofides, Y. Cohen, Energy Consumption Optimization of Reverse Osmosis Membrane Water Desalination Subject to Feed Salinity Fluctuation, Ind. Eng. Chem. Res. 48 (2009) 9581–9589. https://doi.org/10.1021/ie900729x.

[63] M.M. Yazdi, CRAN - Package topsis, (2013). https://cran.r-project.org/web/packages/topsis/index.html (accessed December 28, 2019).

[64] B.C. Ricci, Biorreator anaeróbio osmótico acoplado à destilação assistida por membranas como alternativa para potabilização de esgoto doméstico, Tese de Doutorado, Universidade Federal de Minas Gerais, 2019.

[65] R.W. Holloway, A. Achilli, T.Y. Cath, The osmotic membrane bioreactor: a critical review, Environmental Science: Water Research & Technology. 1 (2015) 581–605. https://doi.org/10.1039/C5EW00103J.

[66] M. Ramezanianpour, M. Sivakumar, An analytical flux decline model for membrane distillation, Desalination. 345 (2014) 1–12. https://doi.org/10.1016/j.desal.2014.04.006.

[67] D.L. Perry, Handbook of inorganic compounds, 2nd ed., CRC Press, Boca Raton, 2011. http://www.crcnetbase.com/isbn/9781439814628 (accessed April 2, 2020).

[68] DDB, Vapor Pressure of Acetic acid from Dortmund Data Bank, Dortmund Data Bank. (2019). http://www.ddbst.com/en/EED/PCP/VAP_C84.php (accessed January 12, 2020).

[69] H. Lee, S.-J. Im, J.H. Park, A. Jang, Removal and transport behavior of trace organic compounds and degradation byproducts in forward osmosis process: Effects of operation conditions and membrane properties, Chemical Engineering Journal. 375 (2019) 122030. https://doi.org/10.1016/j.cej.2019.122030.

[70] A.R.D. Verliefde, S.G.J. Heijman, E.R. Cornelissen, G. Amy, B. Van der Bruggen, J.C. van Dijk, Influence of electrostatic interactions on the rejection with NF and assessment of the removal efficiency during NF/GAC treatment of pharmaceutically active compounds in surface water, Water Research. 41 (2007) 3227–3240. https://doi.org/10.1016/j.watres.2007.05.022.

[71] C.F. Couto, M.C.S. Amaral, L.C. Lange, L.V. de S. Santos, Effect of humic acid concentration on pharmaceutically active compounds (PhACs) rejection by direct contact membrane distillation (DCMD), Separation and Purification Technology. 212 (2019) 920–928. https://doi.org/10.1016/j.seppur.2018.12.012.

[72] K.C. Wijekoon, F.I. Hai, J. Kang, W.E. Price, T.Y. Cath, L.D. Nghiem, Rejection and fate of trace organic compounds (TrOCs) during membrane distillation, Journal of Membrane Science. 453 (2014) 636–642. https://doi.org/10.1016/j.memsci.2013.12.002.

[73] R. Valladares Linares, V. Yangali-Quintanilla, Z. Li, G. Amy, Rejection of micropollutants by clean and fouled forward osmosis membrane, Water Research. 45 (2011) 6737–6744. https://doi.org/10.1016/j.watres.2011.10.037.

Chapter 3: Improving hybrid mesophilic anaerobic osmotic membrane bioreactor - membrane distillation treatment of municipal sewage by using $MgCl_2$ as draw solute: low reverse salt flux and high organic matter, nutrient and estrogenicity removals

Abstract: A submerged hybrid forward osmosis (FO) - membrane distillation (MD) module integrated into an anaerobic bioreactor (AnOMBR-MD) was investigated with the objective of treating municipal sewage containing pharmaceutical drugs and estrogenic activity. A $MgCl_2$ solution (2.1 mol L^{-1}) was used as draw solution (DS), because of its low diffusivity to the mixed liquor. After 32 days of operation, FO and MD permeate water fluxes reduced 82 and 67%, due to organic and inorganic membrane fouling. MD salt rejection was higher than 99.6% and more than 90% of dissolved organic carbon was removed by the AnOMBR-MD. $P\text{-}PO_4^{3-}$ was below the detection limit (0.003 mg L^{-1}) in all DS and distillate samples. $N\text{-}NH_4^+$ in distillate was 5 mg L^{-1} at the end of operation, when the FO-MD rejection was >93%. The impact of the rapid salinity build-up on the conversion capacity of sludge microorganisms was observed, with an increase in soluble microbial products and reduction of estrogenic compounds removal. PhACs removal was higher than 95%, except for ketoprofen that presented a removal of 87%. The AnOMBR-MD removed > 99.97% of estrogenic activity, resulting in a distillate with 0.14 ng L^{-1} E2-eq. AnOMBR-MD treatment promoted reduction in environmental and human health risks from high to low, and carcinogenic risks from unacceptable to negligible, considering estrogenic activity.

Keywords: micropollutants; wastewater treatment; YES assay; risk assessment.

1 Introduction

Endocrine disrupting compounds (EDCs) are defined by the World Health Organization as exogenous substances or mixtures that alter the functions of the endocrine system, causing adverse health effects in an organism, its progeny or populations [1]. EDCs can be natural substances, such as the estrogen 17β-estradiol (E2), or synthetic chemicals, such as bisphenol-A, nonylphenol, pesticides or pharmaceutically active compounds (PhACs) [2,3].

The presence of PhACs in the aquatic environment has been reported in several studies [4–10]. Some of these PhACs are also estrogenic compounds that may have adverse effects on human beings, such as breast and prostate cancer incidence, and on aquatic organisms, such as feminization of male fish [11,12].

In vitro assays are bioanalytical tools used to evaluate samples based on their biological activity [13]. The yeast estrogen screen (YES) is one of the most widely reported *in vitro* assays for evaluating estrogenic compounds [14]. The YES assay has high sensitivity and the interactions of EDCs, even at low concentrations, can be determined, highlighting its importance in assessing potential estrogenicity in waters and wastewaters [15]. It is also a useful tool for assessing the risk associated with EDCs, considering both their potential hazardous effects and exposure levels [16].

The main pathway for PhACs to reach water bodies is municipal sewage treatment plants (STPs) discharges [17–19]. The removal of recalcitrant PhACs is limited in conventional STPs since their objective is to remove biodegradable organic matter and nutrients, [20]. Therefore, there is a need for advanced technologies to reduce PhACs concentrations in treated wastewaters and, consequently, reduce the impacts caused in the environment. Membrane bioreactors (MBR) have shown promising results in removing PhACs. MBR have the benefits of biological treatment but allow a higher solids concentration and sludge residence time, which improve not only the removal of organic matter and nutrients but also the biodegradation of recalcitrant compounds [21,22]. However, MBR using microfiltration or ultrafiltration membranes have high energy consumption, high propensity to fouling, and low efficiency in removing dissolved compounds [23].

Microfiltration or ultrafiltration is replaced by forward osmosis (FO) in osmotic membrane bioreactors (OMBR), overcoming some of the challenges of the membrane bioreactor. OMBR have emerged as an attractive process for treating wastewaters containing PhACs [24,25] due to the high rejection of dissolved compounds by the non-porous forward

osmosis (FO) membrane. FO is a separation process that uses osmotic pressure gradient ($\Delta\pi$) across the semipermeable membrane [26] and is a less energy consuming and less severe fouling membrane process, since hydraulic pressure is not used [27]. Moreover, anaerobic digestion with FO process (AnOMBR) can reduce the energy demand even more [28].

The diluted draw solution (DS) must be reconcentrated to maintain the osmotic pressure gradient and to recover permeate water. Membrane distillation (MD) is a suitable alternative for DS reconcentration because it has low capital cost and operating pressures, is not affected by salt concentration and produces high quality water [29,30]. The driving force of the MD process is the vapor pressure gradient, resulted from the temperature difference. The hydrophobic membrane only allows the passage of vapor, retaining the non-volatile contaminants [31].

Ricci et al. [32] developed a submerged FO-MD hybrid module to compose an AnOMBR-MD for municipal sewage treatment and used NaCl as solute, obtaining 97.5% rejection of micropollutants. A high reverse salt flux (Js) was observed, increasing salinity in the mixed liquor (ML), due to NaCl diffusivity from the DS to the ML. Arcanjo et al. [33] showed that among five different solutes (NaCl, $MgCl_2$, sodium acetate, magnesium acetate, EDTA-Na_2) tested for the FO-MD hybrid module, $MgCl_2$ presented lower J_s, which also improved PhACs membrane rejection. Therefore, the use of $MgCl_2$ as a draw solute could reduce salinity build-up in the AnOMBR-MD and the impact on microbial activity, improving overall removal efficiency of PhACs in long-term operation. Furthermore, the reverse salt flux containing Mg^{2+} could enhance the recovery of nutrients (PO_4^{3-} and NH_4^+) as struvite ($MgNH_4PO_4.6H_2O$), which is an eco-friendly technology for sustainable nutrient management [34].

Some papers have reported the use of $MgCl_2$ in the DS. Qiu and Ting [35] operated an aerobic OMBR for treating a synthetic wastewater and found a better performance when $MgCl_2$ was used as DS compared to NaCl. At the beginning of the operation with each salt, NaCl presented a higher flux, but due to the significant increase in mixed liquor salinity, permeate flux decreased faster than with $MgCl_2$ [35]. Also, the $MgCl_2$ concentration increased the recovery of P-PO_4^{3-} from the mixed liquor. Chang et al. [36] also used $MgCl_2$ as draw solute in an aerobic OMBR-MD combined with microfiltration (MF) extraction in treatment of a synthetic wastewater. They showed that P-PO_4^{3-} could be efficiently recovered from MF permeate as struvite, reducing electrical conductivity in the mixed liquor. Khan et al. [37] concluded that organic solutes (magnesium and sodium acetates) had greater advantages over

inorganic solutes (NaCl, $MgCl_2$ and $CaCl_2$) in an OMBR for treating a synthetic municipal sewage. However, MD is not a suitable process to recover a DS composed of these organic solutes, since acetate is volatile [33]. Nevertheless, the use of a DS composed of $MgCl_2$ in an anaerobic OMBR still needs to be explored.

Thus, the performance of an AnOMBR-MD, using $MgCl_2$ as draw solute, for the treatment of municipal sewage containing PhACs was investigated in terms of permeate fluxes, organic matter and nutrient removals. Estrogenic activity and environmental and human health risks reduction were also assessed.

2 Material and methods

2.1 Feed wastewater and draw solution

Synthetic wastewater, simulating municipal sewage, was prepared according to Mockaitis et al. [38]. The components of the synthetic wastewater, presented in Table S1 (supplementary material – Appendix C), were added to dechlorinated tap water. The synthetic wastewater was spiked with 2 μg L^{-1} of 7 PhACs (17α-ethinylestradiol, betamethasone, fenofibrate, fluconazole, ketoprofen, loratadine and prednisone) and used as feed solution for the AnOMBR-MD.

Anaerobic sludge was collected from a UASB unit, at the Onça municipal sewage treatment plant, located in Belo Horizonte, Minas Gerais, Brazil. The sludge was fed with the synthetic wastewater until inoculation in the bioreactor.

Draw solution (DS) was composed of $MgCl_2$, at a concentration of 2.1 mol L^{-1}, to generate an osmotic pressure of 164.5 bar.

2.2 Experimental setup

The AnOMBR-MD system (Figure 1) used in this study consisted of an FO-MD hybrid module submerged in a bioreactor tank with working volume of 4.5 L, and 3 tanks for the feed solution (FS), DS and distillate. The system included five diaphragm pumps (2 for DS, 1 for distillate, 1 for heated water and 1 for cold water recirculation). DS and distillate tanks were placed on digital scales connected to a computer, to monitor the changes in their masses. Temperature sensors were placed in DS, distillate and bioreactor tanks. Three rotameters were used to monitor and control circulation flowrate. A conductivity probe was placed in the distillate tank. The FO-MD module was presented for the first time by Ricci et al. [39] and was

composed of three compartments for recirculation of DS in the two outer compartments, and distillate recirculated counter-currently in the middle compartment,. Each compartment was separated and sealed by four flat-sheet membranes: two FO membranes placed on the outer faces, with the active layer facing the FS; and two MD membranes on the inner faces. The FO membranes used in the experiments were composed of cellulose triacetate (CTA) and purchased from Hydration Technology Innovations (Albany, OR, USA). The hydrophobic MD membranes with a pore size of 0.2 µm, purchased from Sterlitech Corporation (Kent, WA, USA), were composed of polytetrafluoroethylene (PTFE) laminated on a polypropylene layer membrane. Each membrane had an area of 132 cm^2. One heating system and a chiller were used to control DS and distillate temperatures, respectively. Feed flow was controlled by an electrical panel and a sensor level in the bioreactor tank. When mixed liquor level decreased, the metering pump was activated and feed solution was pumped to the bioreactor. To provide completely mixed conditions, two magnetic stirrers were used in the bioreactor tank and a mechanical stirrer was used in the feed tank.

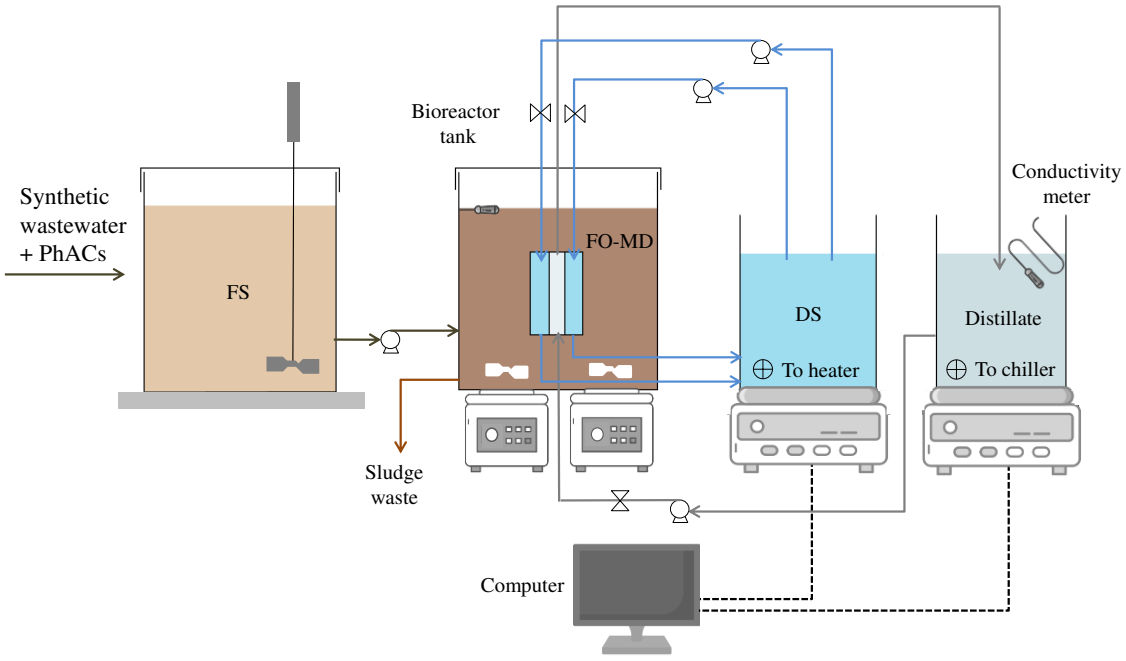


Figure 1 - AnOMBR-MD experimental apparatus.

2.3 Experimental procedure

The system was inoculated with the anaerobic sludge to reach a mixed liquor volatile suspended solids (MLVSS) concentration of 10 g L^{-1}. The operation started with 5 L of DS and 3 L of distillate (deionized water) in each tank. The circulation rate and temperature for DS

were 75 L h^{-1} and 45 °C, respectively. For distillate, these values were 80 L h^{-1} and 25 °C. The synthetic wastewater spiked with PhACs was added to the feed solution tank every 2 days. The hydraulic retention time (HRT) and the organic loading rate were 10.5 days and 0.0419 kg chemical oxygen demand (COD) m^{-3} d^{-1}, respectively. The solids residence time (SRT) was maintained at 45 days.

The AnOMBR-MD was operated under continuous flow for 32 days and the changes in weight of DS and distillate were recorded by a computer in 5 min intervals. Five days each week the temperature of each tank was recorded and samples from feed solution, sludge, DS and distillate were collected to measure their pH and conductivity. Samples were also collected periodically for physicochemical characterization and analyses of soluble microbial products (SMP) and extracellular polymeric substances (EPS), PhACs and estrogenic activity.

2.4 Analytical methods

The samples were characterized according to the Standard Methods for the Examination of Water and Wastewater [40], by quantifying pH (4500-H^+), conductivity (2510), DOC (5310 B, Shimadzu TOC-VCPH analyzer), COD (5220 D), TSS and VSS (2540 D and E), alkalinity (2320 B), P-PO_4^{3-} (4500-P D), N-NH_4^+ (4500-NH_3 B and C), turbidity (2130 B), color (2120 C) and chloride (4500-Cl^-). Magnesium and calcium were determined by hardness (2340 C). Volatile fatty acids (VFA) were quantified according to Kapp [41,42]. SMP and EPS from sludge sample were characterized as protein and carbohydrate fractions [43,44]. For SMP and EPS extraction, 50 mL of sludge were centrifugated at 4450 x g for 10 min, the supernatant was collected as SMP and the sludge pellets were resuspended with 50 mL of 0.05% NaCl solution and heated to 80 °C in a water bath for 10 min [45]. Following, the solution was centrifugated at 4450 x g for 10 min, and the supernatant corresponded to EPS.

The concentration of $MgCl_2$ in the ML, DS and distillate tanks was estimated from electrical conductivity (EC) and temperature measurements, applied to a multiple linear regression calibration curve.

The fouled membranes were characterized using scanning electron microscopy (SEM) using a FEI Quanta 200 scanning microscopy (Hillsboro, OR, USA) and energy dispersive spectroscopy (EDX) using a FIB Quanta FEG 3D. Before scanning, samples were fixed with a carbon tape.

SMP and EPS vertical distribution on the FO membrane surface was also investigated. Foulant was extracted according to Zheng et al. [46]. M1 is the foulant scoured by water,

representing the top layer of the membrane foulant. M2 is the layer of the membrane foulant scraped off by a steel ruler. Finally, total foulant, M3, was extracted by emerging the membrane in water for 30 min. The volume of each sample was completed to 50 mL and extraction followed the same procedure used for ML samples.

PhACs were quantified by liquid-chromatography (Shimadzu Prominence UFLC, Shimadzu, Kyoto, Japan) coupled with mass spectrometry (MicrOTOF-QII, Bruket Daltonics, Bremen, Germany) (LC-MS). The method used to quantify the PhACs is described in detail in Ricci et al. [39] and Faria et al. [47], including recoveries and detection limits.

2.5 Estrogenic activity quantification

2.5.1 Samples treatment

The liquid samples collected from the AnOMBR-MD were filtered through a 0.45 µm cellulose nitrate membrane (Unifil - 510.047) and acidified to pH 3 with H_2SO_4. Solid phase extraction (SPE) on C18 cartridges (500 mg/6 mL, Agilent Technologies) was carried out as described by do Nascimento et al. [48]. The cartridges were conditioned with 3 x 2 mL de hexane, 1 x 2 mL de acetone, 3 x 2 mL de methanol and 5 x 2 mL of deionized water at pH 3. The samples passed through the cartridges at approximately 10 mL min^{-1}, under vacuum, and were dried for 20 min. The analytes were eluted with 4 mL of acetone and the solvent was evaporated. The dried extracts were kept at - 20 °C until used in the YES assay.

The sludge samples were prepared as described by Martín et al. [49], with modifications. Fifty mL of sludge was collected from the AnOMBR-MD and centrifugated at 4450 x g or 10 min. The supernatant was used in SPE. About one g of the sludge pellets was extracted with 5 mL of methanol and shaken for 30 s in a vortex mixer. The samples were then ultrasonicated for 15 min and centrifugated at 4450 x g for 20 min. The supernatant was collected in a glass vial. The procedure was repeated with 2 mL of methanol and 2 mL of acetone. The three supernatants were combined and dried at room temperature. The extract was suspended with 50 mL of deionized water, filtered in a 0.45 µm cellulose nitrate membrane, and acidified to pH 3 with H_2SO_4. SPE was carried out following the same procedures used for the liquid samples.

2.5.2 YES assay

The dried extracts were reconstituted with 1 mL of ethanol right before use in YES assay, which followed the methodology proposed by Routledge and Sumpter [50] and Bila et al. [51] with modifications, as described in Arcanjo et al. [52]. The estrogenic activity of the

samples from the AnOMBR-MD was calculated by interpolation from the E2 standard curve and reported as 17β-estradiol equivalents (E2-eq).

2.6 Permeate fluxes and removal efficiency

Permeate fluxes in MD (J_{MD}) and FO (J_{FO}) membranes [kg m^{-2} h^{-1}] were calculated by Eq (1) and Eq (2):

$$J_{MD} = \frac{\Delta m_D}{\Delta t \times A_m} \quad \text{Eq (1)}$$

$$J_{FO} = \frac{\Delta m_{DS}}{\Delta t \times A_m} + J_{MD} \quad \text{Eq (2)}$$

where Δm_D and Δm_{DS} [kg] are the increase in distillate and DS weight, respectively, over a period, Δt [h], and A_m [m^2] is the membrane area.

J_s was calculated by the Eq. (3), proposed by Phillip et al. [53] and Tang et al. [54]:

$$\frac{J_{FO}}{J_s} = \frac{\mathrm{A}}{\mathrm{B}} \times n \times R \times T \quad \text{Eq (3)}$$

where A and B are the water and salt permeability coefficient for the FO membrane, estimated by Arcanjo et al. [33], equal to 3.23 x 10^{-12} m s^{-1} Pa^{-1} and 5.38 x 10^{-8} m s^{-1}, respectively, n is the number of species that the draw solute dissociates into, in the case of $MgCl_2$, n is equal to 3, R is the gas constant and T is the absolute DS temperature.

The MD salt rejection ($R_{salt,MD}$) was calculated by Eq (4):

$$R_{salt,MD} = \frac{C_{DS} - C_{p,MD}}{C_{DS}} x\ 100 \quad \text{Eq (4)}$$

where C_{DS} and $C_{p,MD}$ are the concentrations of Mg^{2+} or Cl^- in the DS and MD permeate, respectively.

The removal behavior of the PhACs and estrogenic activity was investigated and the contribution of each mechanism (e.g., biodegradation, biosorption and membrane rejection) was calculated. Mass balance evaluation was described in the supplementary material.

The overall removal efficiency of the AnOMBR-MD was calculated by Eq (5)

$$R_{AnOMBR-MD} = \frac{C_{FS} - C_{p,MD}}{C_{FS}} x\ 100 \quad \text{Eq (5)}$$

where C_{FS} is the contaminant concentration in the feed solution.

The removal efficiency of the bioreactor combined with FO rejection (R_{AnOMBR}) was calculated by Eq (6)

$$R_{AnOMBR} = \frac{C_{FS} - C_{p,FO}}{C_{FS}} x\ 100 \qquad \text{Eq (6)}$$

where $C_{p,FO}$ is the contaminant concentration of the FO permeate.

The rejection by the hybrid FO-MD module (R_{FO+MD}) was calculated by Eq (7)

$$R_{FO-MD} = \frac{C_{ML} - C_{p,MD}}{C_{ML}} x\ 100 \qquad \text{Eq (7)}$$

where C_{ML} [ng L^{-1}] is the contaminant concentration in the mixed liquor.

The biological removal of PhACs and estrogenicity, either by biodegradation or biosorption, was estimated according to the mass balance of the mixed liquor in the bioreactor, as previously described by Qiu et al. [55].

The mass of PhAC or 17β-estradiol equivalent (M_{bio}) removed due to biological process was calculated according to Eq (8):

$$M_{bio} = \sum_{i=1}^{n} C_{FS,i} x V_{FS,i} - \sum_{i=1}^{n} C_{FO,i} x V_{FO,i} - \sum_{i=1}^{n} C_{ML,i} x V_{Wslg,i} + C_{ML,1} x V_R - C_{ML,n} x V_R \qquad \text{Eq (8)}$$

where $C_{FS,i}$ and $V_{FS,i}$ are the concentration of micropollutants and the volume entering the bioreactor, from vthe start of operation to time n. $C_{FO,i}$ and $V_{FO,i}$ are the concentration of the micropollutants and the volume of permeate that passed through the FO membrane. $C_{ML,i}$ and $V_{Wslg,i}$ are the concentration of micropollutants in the mixed liquor supernatant and the volume of waste sludge discharged, respectively. V_R [L] is the bioreactor volume. Thus, the biological removal, at the time n, can be calculated by Eq (9):

$$R_{bio} = \frac{M_{bio}}{\sum_{i=1}^{n} C_{FS,i} x V_{FS,i}} \qquad \text{Eq (9)}$$

The mass of micropollutant removed by biosorption ($M_{biosorp}$) was calculated based on the changes in the sludge phase concentration, as shown in Eq (10):

$$M_{biosorp} = \sum_{i=1}^{n} C_{Slg,i} x V_{Wslg,i} C_{MLSS,i} + C_{Slg,n} x V_R C_{MLSS,n} - C_{Slg,1} x V_R C_{MLSS,1} \qquad \text{Eq (10)}$$

where $C_{Slg,i}$ is the concentration of micropollutant in the sludge phase, in ng $gMLSS^{-1}$, $V_{Wslg,i}$ is the volume of waste sludge discharged, C_{MLSS} is the total suspended solids in the mixed liquor, on day i. $\sum_{i=1}^{n} C_{Slg,i} x V_{Slg,i} C_{MLSS,i}$ is the cumulative amount of micropollutants discharged with the waste sludge.

The biosorption removal ($R_{biosorp}$) was calculated by Eq (11):

$$R_{biosorp} = \frac{M_{biosorp}}{\sum_{i=1}^{n} C_{FS,i} x V_{FS,i}} \qquad \text{Eq (11)}$$

Biodegradation removal is the difference between the biological removal and the biosorption. Therefore, the mass of PhAC or 17β-estradiol equivalent removed by biodegradation (M_{biodeg}) was calculated by Eq (12):

$$M_{biodeg} = M_{bio} - M_{biosorp} \quad \text{Eq (12)}$$

Finally, the biodegradation removal (R_{biodeg}) was determined by Eq (13):

$$R_{biodeg} = \frac{M_{biodeg}}{\sum_{i=1}^{n} C_{FS,i} x V_{FS,i}} \quad \text{Eq (13)}$$

2.7 Thermodynamic calculations with Visual MINTEQ

The speciation of inorganic ions (Ca^{2+}, Mg^{2+}, NH_4^+ and PO_4^{3-}) and the spontaneous precipitation of P-PO_4^{3-} within the bioreactor were calculated using Visual MINTEQ 3.1, a chemical equilibrium model program that contains a mineral species database [56].

The theoretical concentrations of P-PO_4^{3-}, Mg^{2+}, Ca^{2+} and Cl^- were estimated by mass balance, considering the concentration entering the bioreactor and J_s. Following the model proposed by Jia et al. [57], seven minerals were selected as possible species in the model: brucite ($Mg(OH)_2$). brushite ($CaHPO_4.2H_2O$); magnesite ($MgCO_3$); monetite ($CaHPO_4$); nesquehonite ($MgCO_3.3H_2O$); newberyte ($MgHPO_4.3H_2O$); and struvite ($MgNH_4PO_4.6H_2O$). Due to the solution pH and some mineral crystallization rate, the authors excluded some other possibilities, such as hydroxyapatite ($Ca_5(PO_4)_3OH$) and dolomite ($CaMg(CO_3)_2$). The software was run for 5 days of operation (0, 7, 14, 21 and 28) and input data included pH, temperature, alkalinity, DOC, and P-PO_4^{3-}, Mg^{2+}, Ca^{2+} and Cl^- measured in the bioreactor. Theoretical concentration was also calculated, considering the entrance and discharge of ions, during the AnOMBR-MD operation. For Mg^{2+} and Cl^-, the reverse salt flux, calculated by Eq (3), was considered.

2.8 Environmental and human risk assessment

Environmental and human health risks of the municipal sewage and distillate were estimated in relation to estrogenic activity. Eq (14) was used to calculate the acute and chronic environmental risk quotient (RQ).

$$RQ = \frac{MEC}{PNEC} \quad \text{Eq (14)}$$

where MEC is the measured estrogenic activity in E2-eq, and PNEC is the predicted non-effect concentration for aquatic wildlife. According to Caldwell et al. [58], the PNEC for E2 is 5 ng L^{-1} for acute toxicity and 2 ng L^{-1} for chronic effects.

The human health risk was estimated by the hazard quotient (HQ) according to Eq (15). The is the drinking water guideline level (DWGL) values were obtained from Eq (16).

$$HQ = \frac{MEC}{DWGL} \quad \text{Eq (15)}$$

$$DWGL = \frac{TDI\ x\ BW\ x\ f}{DL} \quad \text{Eq (16)}$$

where TDI is the tolerable daily intake for E2, of 7 x 10^{-5} µg kg^{-1} d^{-1} via drinking water for adults [59], BW is the body weight, considered 70 kg, f is the relative contribution of water exposure, considered equal to 100% and DI is the daily intake, set at 2 L d^{-1}.

Also, the incremental lifetime carcinogenic risk (ILCR) was calculated for estrogenic activity [Eq (17)], where EF is the exposure frequency, 365 d per year, ED is the exposure duration, equal to 70 years, AT is the average time, of 25,550 d and CSF is the cancer slope factor, that for E2 is equal to 39 (mg kg^{-1} d^{-1})$^{-1}$ [60].

$$ILCR = \frac{MEC\ x\ DI\ x\ EF\ x\ ED\ x\ CSF}{BW\ x\ AT} \quad \text{Eq (17)}$$

Environmental and human health risk value was considered high for RQ or HQ > 1, medium when 0.1 ≤ RQ or HQ ≤ 1, low when 0.01 ≤ RQ or HQ < 0.1, and negligible when RQ or HQ < 0.01 (European Commission, 1996). The ILCR was classified as unacceptable (ILCR > 10^{-4}) acceptable (10^{-4} < ILCR < 10^{-6}) or negligible (ILCR < 10^{-6}) (EPA, 2015).

3 Results and discussion

3.1 Permeate flux, reverse salt flux and MD salt rejection

Permeate fluxes at the beginning of operation were 2.8 and 1.6 kg m^{-2} h^{-1} for FO and MD membranes, respectively (Figure 2). After 24 h of operation, J_{FO} reduced to 2.2 kg m^{-2} h^{-1} and continued to decline, stabilizing at about 0.5 kg m^{-2} h^{-1}. A different behavior was observed for J_{MD}, which increased slightly until day 3, because of the increase in DS temperature (Figure S1, supplementary material), and then, started to decrease and stabilized in 0.5 kg m^{-2} h^{-1}.

An important factor for the observed reduction in J_{FO} is the high MLVSS concentration maintained in the bioreactor (6.1 ± 1.1 g L^{-1}), which favored the development of slow-growing bacteria, such as methanogenic *Archaea* [61]. Elevated MLVSS are known to contribute to severe fouling and external concentration polarization (ECP) in FO membranes [62]. Higher fluxes were obtained by other authors in submerged AnOMBR operation (3 to 3.5 L m^{-2} h^{-1})

[36,63,64], but at MLVSS in the bioreactors of less than 4.6 g L^{-1}, which may have minimized the effect of ECP on the active layer of the FO membrane. Another cause of J_{FO} reduction was the internal concentration polarization (ICP). ICP resulted in of DS dilution , because of water permeation at the interface between the active layer and the support layer in FO membrane, reducing osmotic pressure [65]. Furthermore, with time, the salinity build-up in the bioreactor (Figure 3), caused by the accumulation of salts from the feed solution and by the reverse salt flux, led to a reduction in the driving force across FO membrane and, thus, J_{FO} decline [64].

Although MD performance is relatively independent of the feed salinity, the concentration and temperature polarization at the membrane surface impact the permeate flux and, as demonstrated by Ricci et al. [39] in the submerged hybrid FO-MD module. In a previous work, $MgCl_2$ concentration at the membrane surface increased 24% in relation to the DS concentration (0.36 mol L^{-1}) [33], as a result of water permeation through the membrane and accumulation of solute. Since the DS concentration was higher, for the same conditions of temperature and recirculation rate, it is expected that the concentration polarization phenomena contributed to J_{MD} decline. The temperature in the DS and distillate bulk was 45.1 ± 0.9 °C and 22.9 ± 1.5 °C (Figure S1, supplementary material), respectively, resulting in a temperature gradient of 22 °C for MD process. Nevertheless, temperature polarization, which is the reduction of temperature at the membrane interface on the feed side and increment on the distillate side, reduced the effective temperature difference across the MD membrane, leading to lower J_{MD} [66].

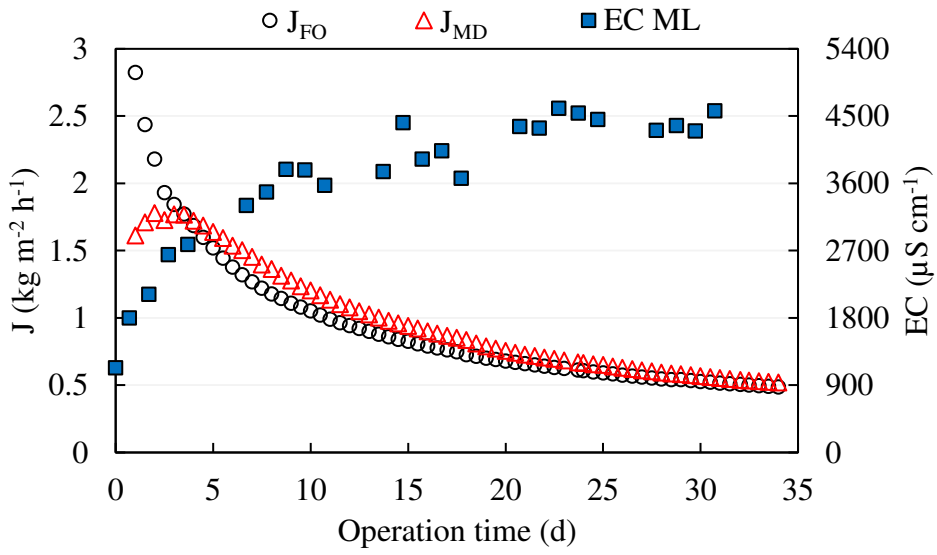


Figure 2 - Permeate flux in FO and MD and electrical conductivity in the ML.

$MgCl_2$ was chosen as draw solute because of its low reverse salt flux (J_s), among other advantages. The concentrations of Mg^{2+} and Cl^- in the bioreactor the sludge samples (Figure 3), were initially 5.8 mg L^{-1} and 177 mg L^{-1}, respectively. Their concentrations increased until day 21, stabilizing at almost 100 mg L^{-1}, for Mg^{2+}, and 1000 mg L^{-1}, for Cl^-. The same pattern was observed for electrical conductivity (EC), that increased from 1100 µS cm^{-1} to 4400 µS cm^{-1}, over 21 days of operation, and maintained the latter value until the end of the operation. These results indicate that the sludge wasting to regulate sludge retention time at 45 d, was enough to reduce salinity build-up in the bioreactor. For the same operation time, Ricci et al. [32], who used NaCl to compose DS, found a conductivity of 43 mS cm^{-1} NaCl, evidence that, indeed, $MgCl_2$ has a much lower J_s that reduces the salinity impact on bioreactor microbial activity and DS replenishment costs. J_{FO} and the AnOMBR-MD performance were not affected by salinity build-up. Differently from Ricci et al. [32], the continuous decline of J_{FO} after 21 d must be attributed to fouling and ECP, since the osmotic pressure in the ML stabilized during this period.

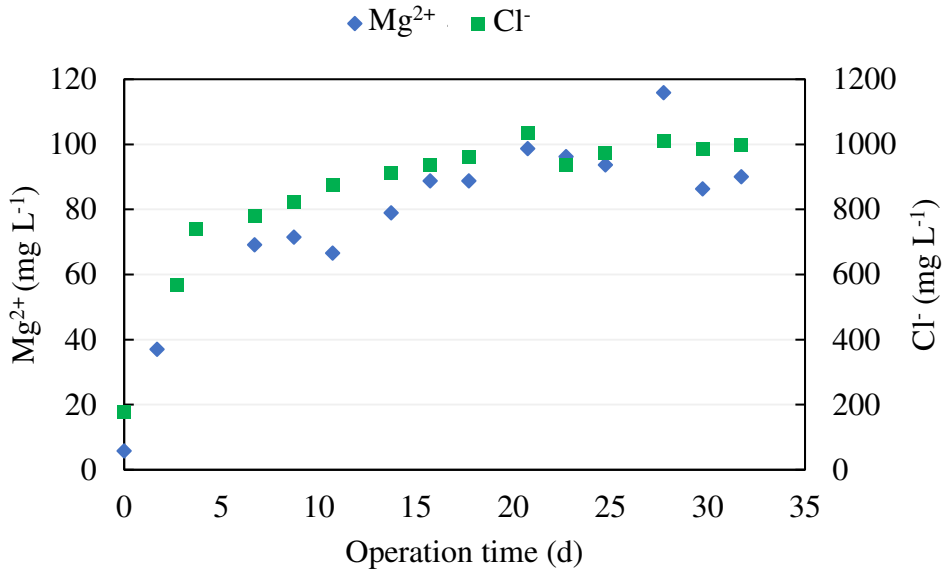


Figure 3 - Salinity build-up in the mixed liquor: Mg^{2+} and Cl^- concentration.

DS concentration started at 194.6 g L^{-1} (Figure 4a), considering the sum of Mg^{2+} and Cl^-, and on the 2nd day of operation, solute concentration declined, reaching 114 g L^{-1}, since J_{FO} was higher than J_{MD}. Then, salt concentration increased, due to J_{FO} being a little lower than J_{MD} and from day 10 to day 32, DS concentration was constant, around 180 g L^{-1} since the permeate flux in FO and MD were similar.

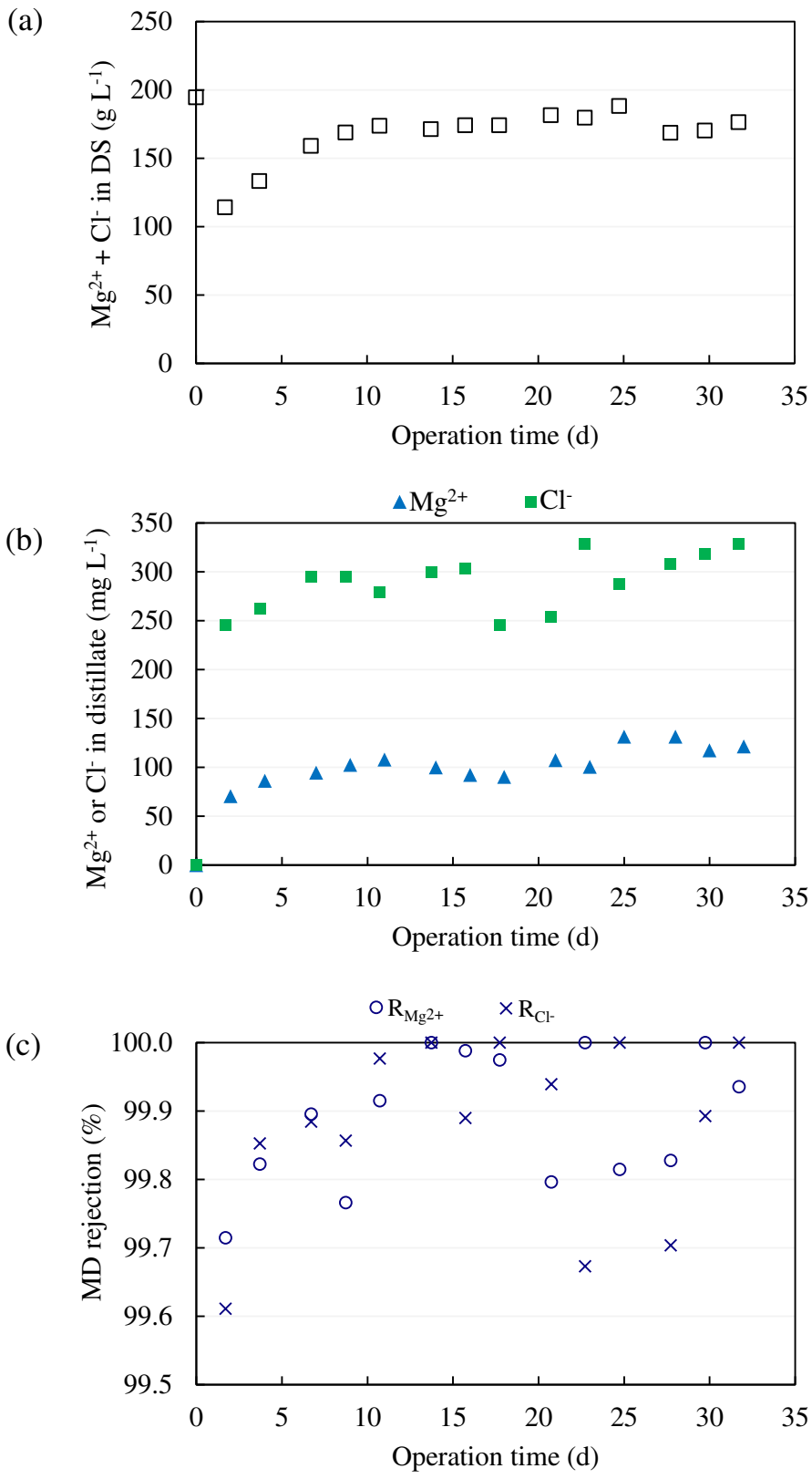


Figure 4 - (a) Sum of Mg^{2+} and Cl^- concentration in the DS; (b) Mg^{2+} and Cl^-concentration in the distillate; and (c) salinity rejection by the MD membrane.

Despite the high salt concentration on the MD membrane surface, distillate Mg^2concentration was below 130 mg L^{-1}, stabilizing after 25 d (Figure 4b). Since Cl^- has a smaller hydrated radius than Mg^{2+}, Cl^- concentration in distillate was higher than Mg^{2+}, remaining between 250 and 350 mg L^{-1}. Nevertheless, MD membrane presented a salt rejection higher than 99.6% for both Mg^{2+} and Cl^- (Figure 4c).

3.2 Characterization of SMP and EPS

From the beginning of AnOMBR-MD operation until day 10, there was a significant decrease in MLTSS and MLVSS (Figure 5). As shown in Figure 3, a continuous increase in the bioreactor salinity could have affected the anaerobic consortium of microorganisms. Salinity build-up has a severe impact in osmotic membrane bioreactors [67]. Moreover, the convective heat transfer from the heated DS to the FO membrane and, from the latter to the ML resulted in the increase of the bioreactor temperature from 28.6°C to 40 °C, in just 1.5 h of operation (Figure S1, supplementary material). The average ML temperature was 38.1 ± 1.8 °C during bioreactor operation, which can benefit micropollutants removal, even under high saline conditions [68]. The combined influence of temperature and salinity on AnOMBR-MD performance should also be considered, especially if the MD module is submerged. Nevertheless, after 10 days, even with the increase in $MgCl_2$ concentration, and subsequent stabilization in the ML, MLVSS did not change significantly, being maintained at 6.1 ± 1.1 g L^{-1}. Furthermore, sludge particle size, considering both average diameter and D95 (Figure S2, supplementary material), also decreased at the beginning of the operation, with no significant change after day 9.

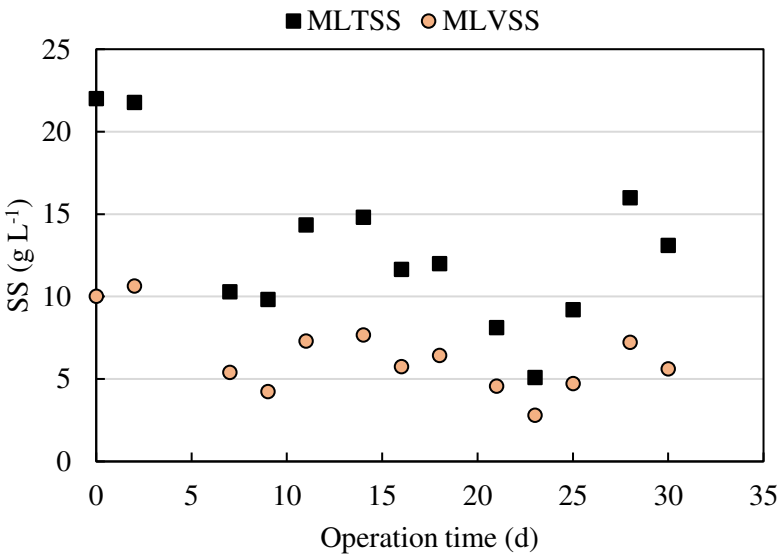


Figure 5 - Mixed liquor TSS and VSS in the bioreactor.

As illustrated in Figure 6a, carbohydrates content in SMP was less affected by the salinity build-up with the operation time than proteins. The increase in temperature and salinity also impacts the release of SMP and EPS, which are the primary source of membrane foulant [69]. Chen et al. [63] observed the same behavior in an AnOMBR operated with 0.5 mol L^{-1} NaCl as DS. However, they found lower concentrations than in the present study (maximum of 6.2 mg L^{-1} for carbohydrates and 49.3 mg L^{-1} for proteins), which could be related to the lower MLVSS maintained in their AnOMBR (3.9 to 4.6 g L^{-1}), thus, less SMP were produced. No relationship between conductivity and EPS carbohydrate and protein contents was found in the present work. Carbohydrate was detected at concentrations of 4.2 ± 1.9 mg $gMLVSS^{-1}$, while protein reached higher values, of 29.0 ± 5.3 mg $gMLVSS^{-1}$, with a decrease after day 13, increasing again on day 29 (Figure 6b). Luo et al. [70] found out that even though the EPS concentration increased with salt loading in a saline aerobic MBR, at the end of operation (70 days) EPS content decreased. This could be a result of the transformation of EPS into SMP due to salinity build-up [71,72], as observed in the present work.

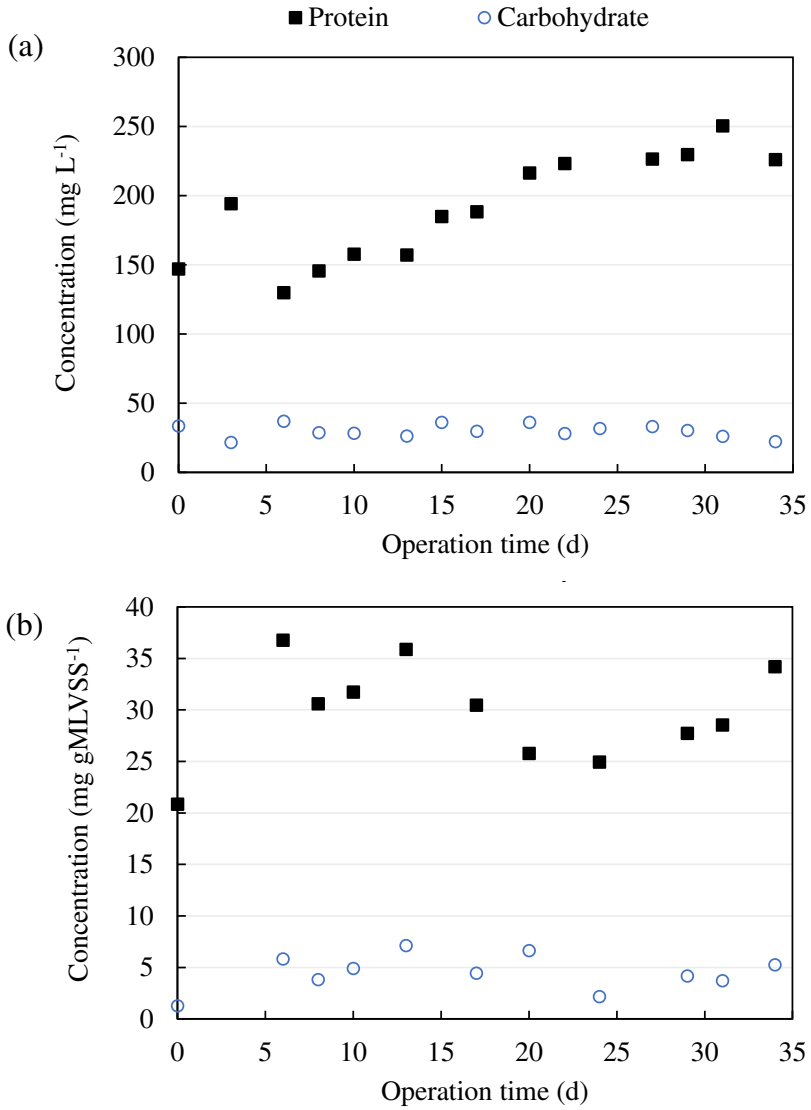


Figure 6 - Variation of (a) SMP and (b) EPS in the mixed liquor.

The concentration of SMP and EPS deposited on the FO membrane surface after 32 days of operation is presented in Figure 7. EPS concentration was higher than SMP, for both proteins and carbohydrates. thus, the reduction in J_{FO} was more pronounced due to EPS released at the membrane surface. Also, more than 50% of the carbohydrates and proteins were removed by just scouring the membrane with water (M1 compared to M3). Physical cleaning, like air scouring with biogas produced in the anaerobic digestion and osmotic backwash, could effectively recover the FO permeate flux. Valladares Linares et al. [73] proposed a cleaning protocol for a FO membrane and obtained a high flux recovery (89.5%) using air scouring for 15 min. Osmotic backwash did not recover the permeate flux and chemical cleaning with EDTA and Alconox were the most efficient in removing the fouling. Nevertheless, the cleaning

protocol for an AnOMBR-MD should be investigated, to guarantee competitive permeate fluxes.

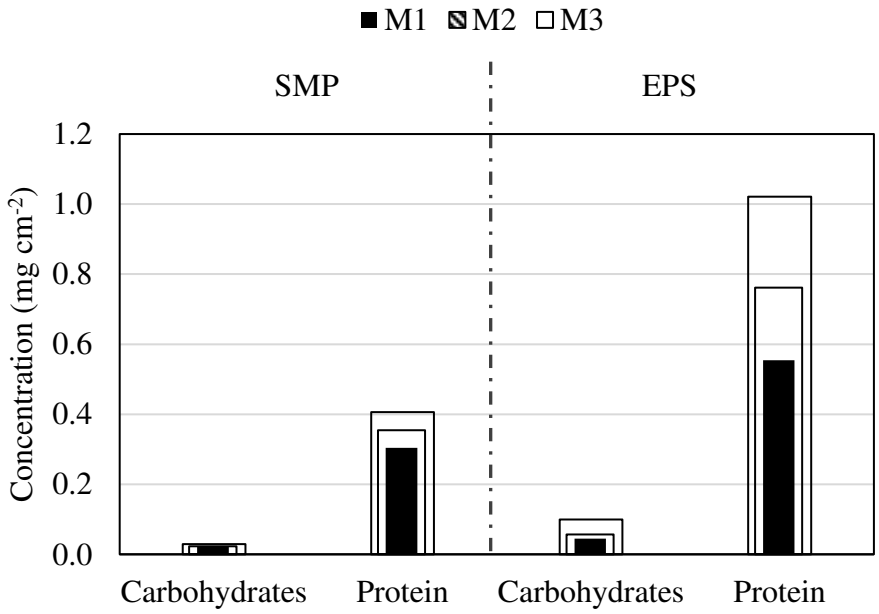


Figure 7 - SMP and EPS characterization at the membrane surface. M1: top layer of the membrane foulant; M2: upper layer of the membrane foulant; and M3: total foulant.

3.3 FO and MD membrane fouling

The observed reduction in J_{FO} and J_{MD} was also related to membrane fouling. Visual examination confirmed an expressive cake layer in the FO membrane, formed mainly by biofouling (Figure S3, Supplementary Material). From the SEM images of the virgin (Figure 8a) and used (Figure 8b) FO membrane, deposition of a fouling layer was observed. Furthermore, it was possible to identify inorganic deposition on the FO membrane surface (Figure 8c), and the EDX results showed that oxygen (52.5%), magnesium (25.5%) and chlorine (22.0%) were the principal elements in the foulant layer. Since the pristine CTA membrane did not present Mg and Cl [74], the presence of Mg and Cl in the membrane can be associated with ICP, ECP and J_s, from the DS. Draw solution components were also observed on the FO membrane from an OMBR, in the study of Nguyen et al. [30]. Therefore, besides the impact of salinity build-up on biological treatment and driving force reduction, J_s is also responsible for membrane fouling.

For the MD membrane, crystal deposition and great pore blocking were observed (Figure 8e and Figure 8f), when compared to the virgin MD membrane (Figure 8d). EDX mapping (Figure 9) showed that, besides fluorine and carbon, which are part of the PTFE structure, fouling was formed by carbon, oxygen and magnesium, indicating both biofouling

and precipitation of magnesium from the draw solute. Carbon tapes used to fixe the sample may have also contributed to the carbon found in EDX. Organic and inorganic contaminants accumulate in the DS because of the higher rejection by the MD membrane, which is an undesired consequence of DS regeneration [27].

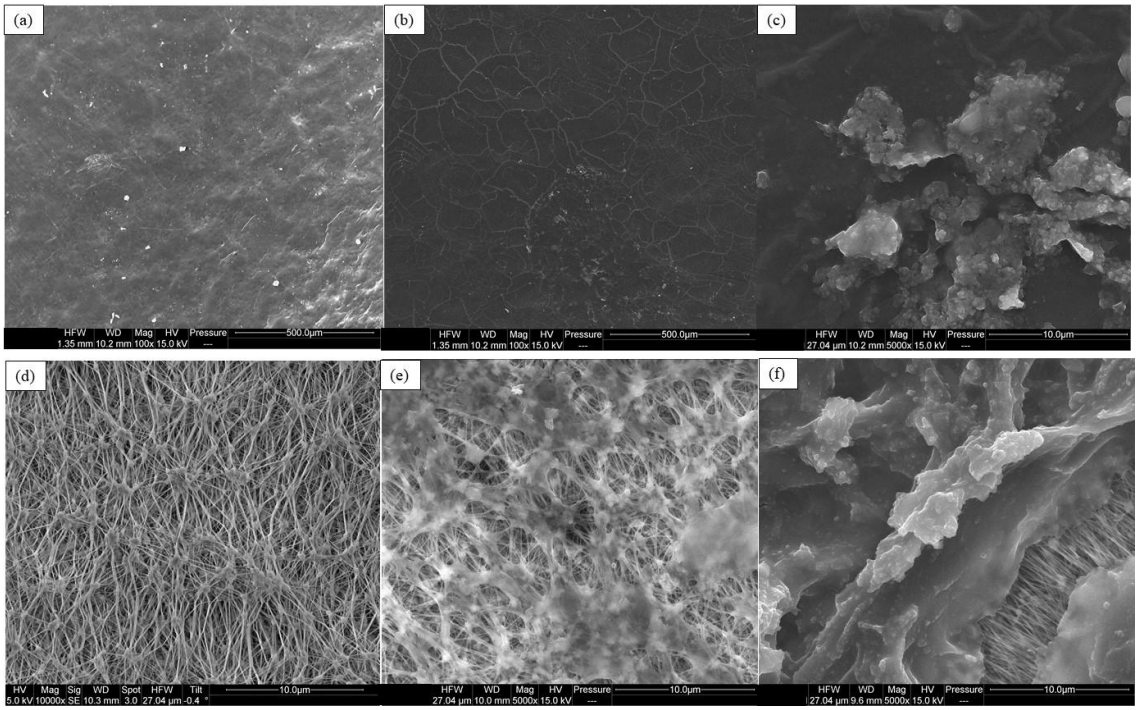


Figure 8 - SEM images for the (a) pristine FO membrane; (b) and (c) used FO membrane; (d) pristine MD membrane; (e) and (f) used MD membrane.

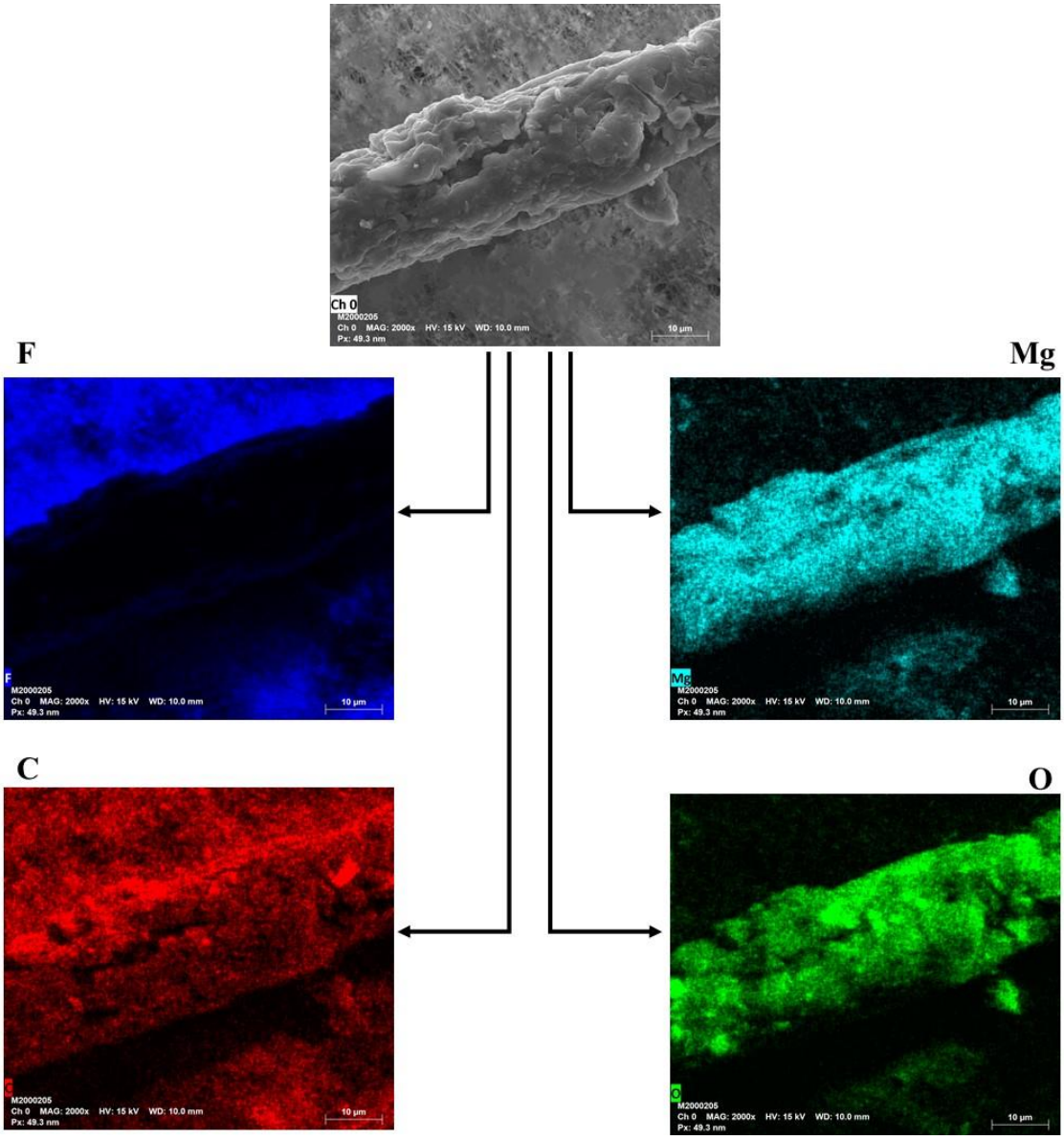


Figure 9 - EDX mapping of the MD membrane after AnOMBR-MD operation. (Blue: fluorine; Cyanide blue: Mg; Red: carbon; and Green: oxygen).

3.4 Alkalinity, volatile fatty acids and pH

Alkalinity values greater than 300 mg L^{-1} $CaCO_3$ were found for the sludge samples throughout AnOMBR-MD operation (Figure 10a). Alkalinity is an important parameter in anaerobic bioreactors to reduce mixed liquor acidification that directly affects the stability and activity of biomass, especially methanogenic organisms [75–77]. The production of VFA by microorganisms, mainly in the phases of hydrolysis and acidification can contribute to pH reduction in anaerobic treatments [42,78]. VFA concentration in the mixed liquor varied from 153 to 832 mg HAc L^{-1} (Figure 10b), while VFA/alkalinity ratio remained between 0.32 and 0.68 after 7 days, which could indicate some instability in anaerobic digestion [79]. However,

even with high concentrations of VFA in the mixed liquor, much lower than the critical value of 4000 mg L^{-1} [80], the pH remained stable at about 7.8 (Figure S4, Supplementary Material), which demonstrates the capacity of the AnOMBR to reduce the effects of VFA accumulation. This might not be possible in conventional anaerobic MBR, since alkalinity is reduced, due to the passage of carbonates and bicarbonates through microfiltration and ultrafiltration membranes [64].

It is also important to highlight the low concentrations of VFA in the distillate (< 30 mgHAc L^{-1}). Yao et al. [81] used a membrane distillation bioreactor for wastewater reclamation and obtained concentrations of 100 mg L^{-1} VFA in the permeate when the bioreactor temperature was 45 ºC and around 30 mg L^{-1}, at a temperature of 65 ºC. In the AnOMBR-MD, the FO membrane acts as the first barrier to contaminants from the bioreactor and the post-treatment with MD assures the efficiency of the hybrid system in rejecting these compounds.

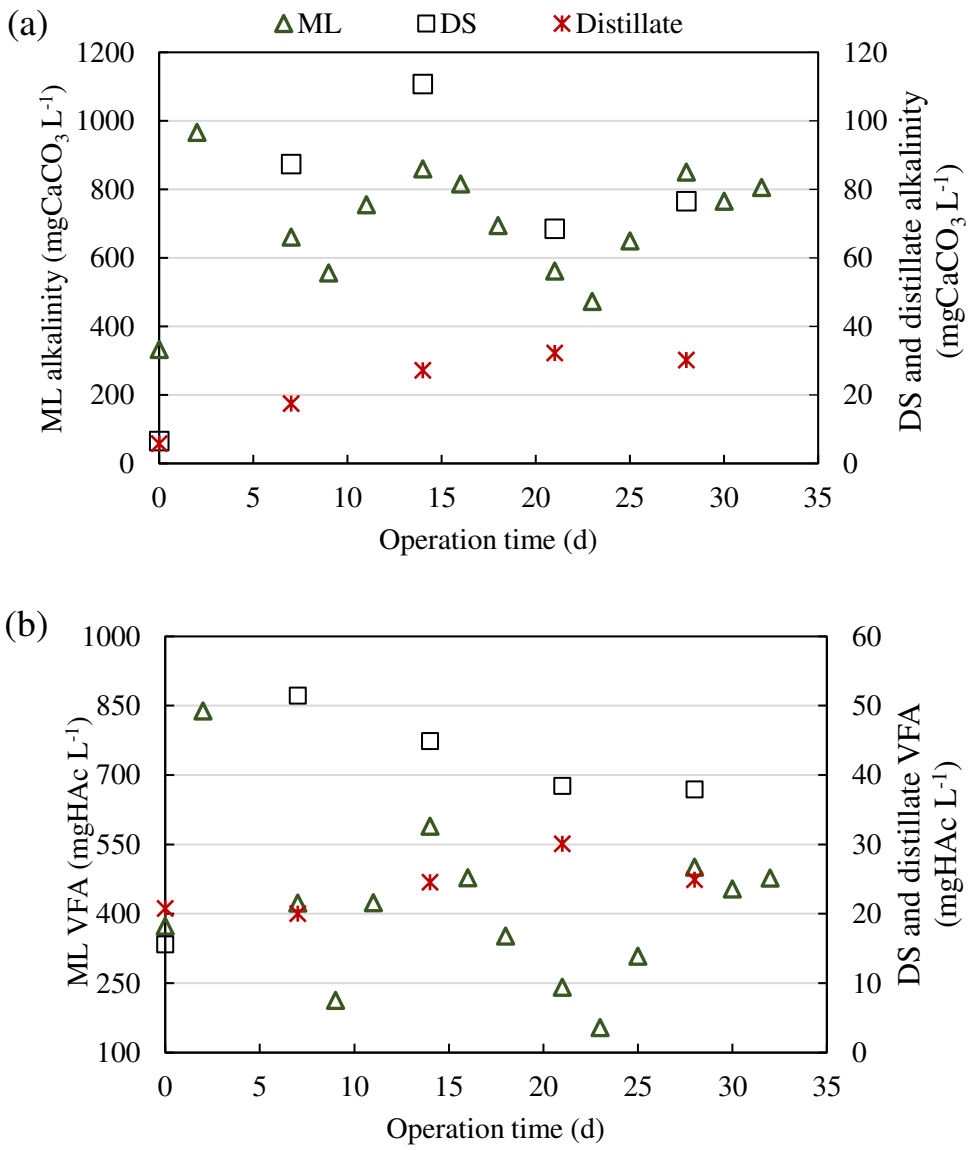


Figure 10 - (a) Alkalinity and (b) VFA during AnOMBR-MD operation.

3.5 Organic matter and nutrients removal

The DOC removal efficiency in the AnOMBR was higher than 75.5% and the DOC concentration in the DS reached 29 mg L^{-1}. The overall DOC removal efficiency ($R_{AnOMBR-MD}$) was higher than 96.3%, until day 15 (Figure 11), with concentrations below 4.5 mg L^{-1} in the distillate. A reduction to about 90% removal was then observed and the DOC concentration in distillate increased to 13 mg L^{-1}. Ricci et al. [32] obtained 97.1% of DOC removal, operating a similar AnOMBR-MD with NaCl as draw solution. Thus, the results found in the present work could be justified by wetting of the distillation membrane which allowed the passage of salts, as discussed in section 3.1, and organic matter, but also by volatile organic compounds produced in the anaerobic process, since they have reduced rejection in the MD process.

Biological removal of DOC (R_{Bio}) was higher than 60%, and no accumulation in the bioreactor was observed, even with the salinity build-up in the bioreactor up to day 21.

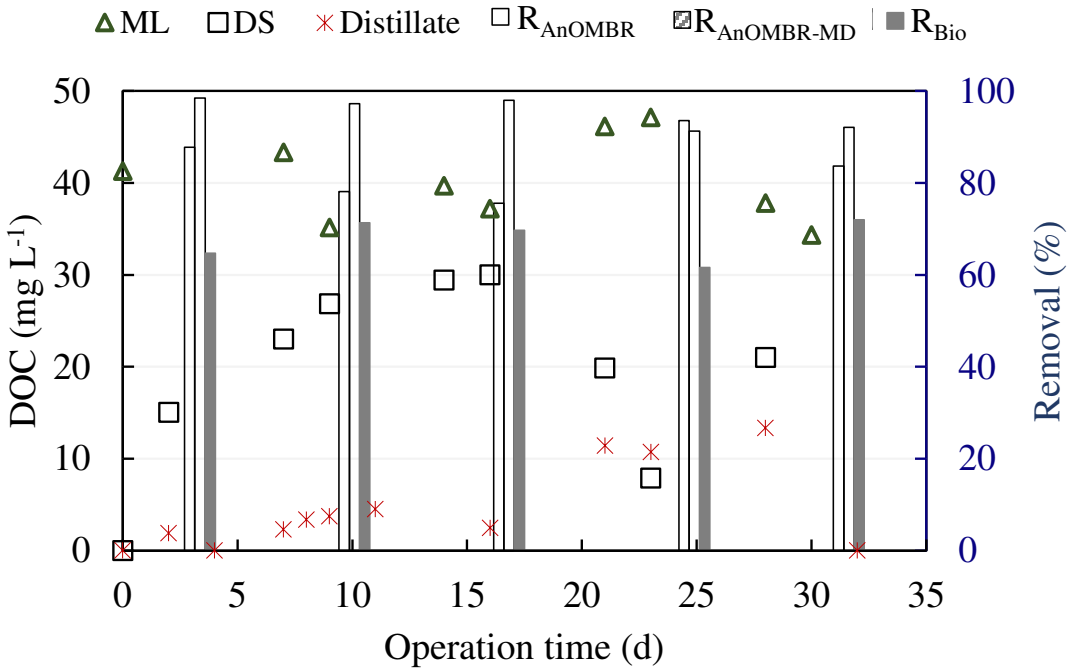


Figure 11 - DOC concentrations and removal efficiency at AnOMBR-MD. (FS concentration: 122.6 mg L^{-1}).

Ammonium nitrogen (N-NH_4^+) concentrations were higher in ML than in the feed solution (Figure 12a). This results from the transformation of organic nitrogen into N-NH_4^+ in the anaerobic process and the rejection by the FO membrane. At the beginning of operation, the concentration of N-NH_4^+ in the DS increased, due to its transfer from ML to DS. When ML concentration reduced, from day 16, N-NH_4^+ in the DS also decreased. The rejection by the FO membrane, calculated considering the ML concentration, was in the range of 58 to 69%. These values agree with those reported in the literature for AnOMBR, from 57 to 86% [82,83]. Considering the DS temperature and pH, approximately 97% of the N-NH_4^+ was in the form of ammonium ion (NH_4^+). Therefore, 3% was present as free ammonia (NH_3) and due to its volatility, it also passed through the MD membrane, and concentration in distillate reached values below 6.2 mg L^{-1}. The hybrid FO-MD module presented higher rejection after 20 days (> 93%), related to the reduction in ML and DS concentration. The use of membrane contactors for ammonia recovery has been reported as an easy alternative to produce fertilizer with high quality, as $(NH_4)_2SO_4$ [84,85]. With the treatment of the DS by membrane contactors, N-NH_4^+ concentration would be reduced, minimizing its passage to the distillate. Also, recovery of struvite from the ML could reduce ammonia transfer to the FO-MD module.

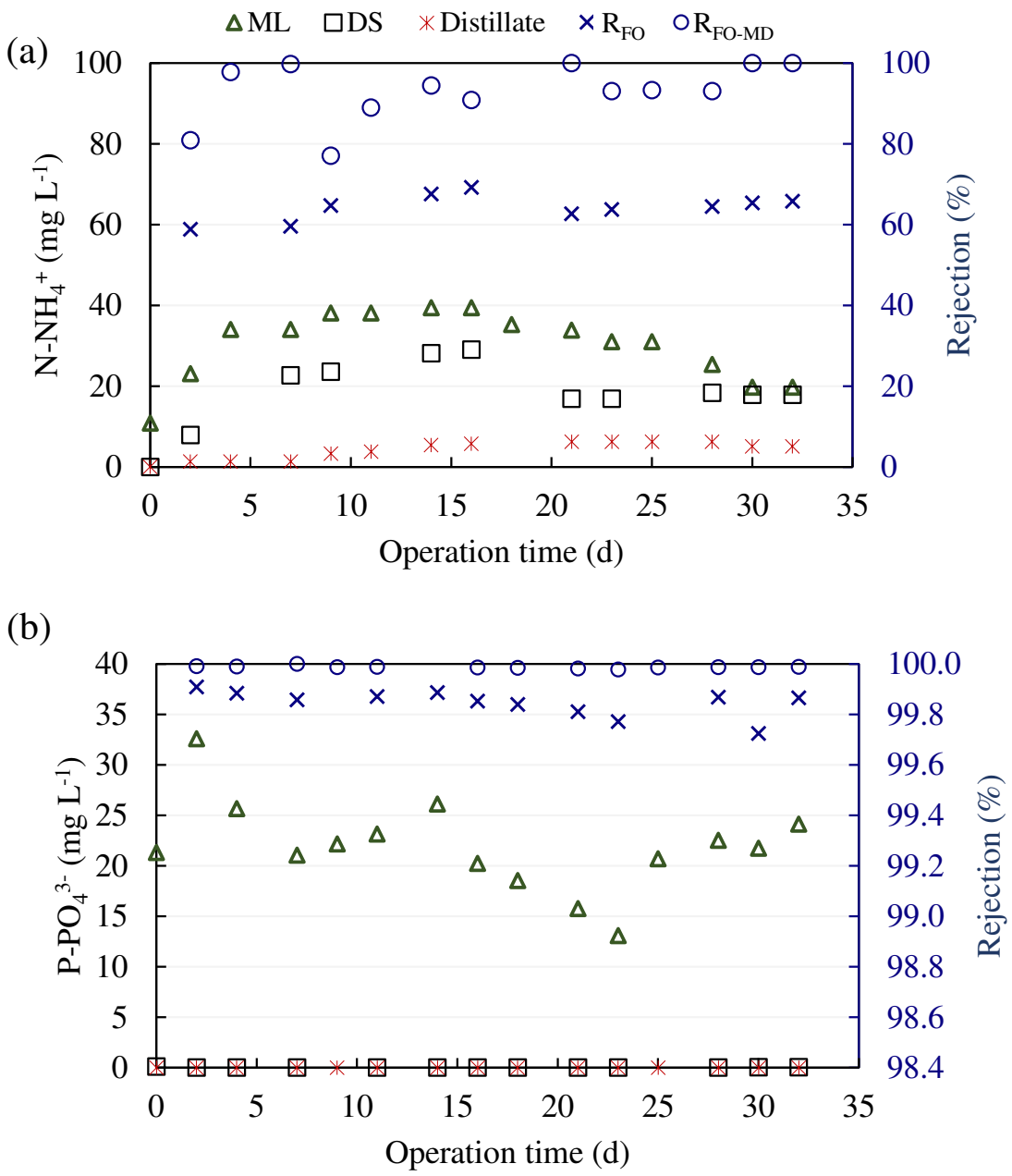


Figure 12 - Concentrations and rejections during AnOMBR-MD operation: (a) N-NH_4^+ and (b) P-PO_4^{3-}. (FS concentration: 29.9 mg L^{-1} P-PO_4^{3-} and 6.4 mg L^{-1} N-NH_4^+).

The phosphorus concentrations in the DS and the distillate were below the detection limit (0.003 mg L^{-1}), and the rejection by the FO membrane was greater than 99.7% (Figure 12b). The AnOMBR-MD system presented total phosphorus (P-PO_4^{3-}) removal of 99.99% during the entire operation, higher than the values reported by other authors who worked with the hybrid FO-MD process, of around 95% [32,82,86]. There was also removal of P-PO_4^{3-} in the bioreactor since the concentration in the ML was below the feed solution (29.9 mg L^{-1}), with a slight increase from day 7 to 14, and again from day 23 to 32.

$P\text{-}PO_4^{3-}$ concentration in the ML supernatant was below the expected value, calculated from the mass balance. The Visual MINTEQ 3.1 model (Table 1) indicated that magnesite, monetite and struvite may have precipitated in the bioreactor, justifying the reduction in PO_4^{3-} as well as $N\text{-}NH_4^+$, after day 16. Gu et al. [64] reported possible precipitation of Ca^{2+}, $P\text{-}PO_4^{3-}$ and other ions on the FO membrane surface during operation of an AnOMBR using NaCl as the draw solute. Since $MgCl_2$ was used in the DS in the present research, Mg^{2+} was also a component of the inorganic scaling, as discussed in Section 3.3. With the high rejection by the FO membrane, it would be possible to enrich the concentration of nutrients at the bioreactor supernatant, and recover nitrogen and phosphorus. Some researchers have reported the recovery of PO_4^{3-} from municipal sewage by aerobic OMBR [35,87,88]. However, the simultaneous recovery of $N\text{-}NH_4^+$ and $P\text{-}PO_4^{3-}$ in the form of struvite ($NH_4MgPO_4.6H_2O$) in the anaerobic OMBR is an attractive alternative, because of accumulation of these nutrients, as well as Mg^{2+}, due to J_s. Furthermore, with continuous recovery of $N\text{-}NH_4^+$ and $P\text{-}PO_4^{3-}$ and consequently reduction of their concentration in the mixed liquor supernatant, scaling could be controlled, and fewer ions would pass through the FO and MD membranes, producing a treated effluent with better quality.

Table 1 - Ion concentrations in the ML and possible precipitate species formed

Parameter	**Operation time (d)**				
	0	7	14	21	28
pH	6.9	7.5	7.8	8.2	8.1
Temperature (°C)	39.5	37.9	36.6	37.7	38.0
Mg^{2+} (mg L^{-1})	5.8	69.1	78.9	98.7	115.9
Mg^{2+} (mg L^{-1}) calculated	0.0	324.4	472.2	552.8	603.7
NH_4^+ (mg L^{-1})	13.8	42.1	47.9	35.4	27.4
Ca^{2+} (mg L^{-1})	20.3	20.3	36.6	16.3	36.6
Ca^{2+} (mg L^{-1}) calculated	20.3	122.3	153.9	176.0	175.3
Cl^- (mg L^{-1})	177.3	780.6	911.0	1034.2	1009.5
Cl^- (mg/L) calculated	0.0	1963.6	2580.6	2792.4	2886.8
P PO_4^{3-} (mg L^{-1})	66.7	65.8	81.6	49.3	70.4
PO_4^{3-} (mg L^{-1}) calculated	66.7	207.0	256.3	283.3	306.7
DOC (mg L^{-1})	41.3	43.3	39.7	46.1	37.8
Alkalinity (mg L^{-1})	332.7	660.6	859.8	561.6	851.2
Solid phase					
Magnesite ($MgCO_3$) (mg L^{-1})	0	171.7	878.4	694.7	1140.6
Monetite ($CaHPO_4$) (mg L^{-1})	0	85.7	159.9	119.1	182.1
Struvite ($MgNH_4PO_4.6H_2O$) (mg L^{-1})	0	0	0	74.3	24.5

3.6 PhACs and estrogenic activity removal

PhACs accumulated in DS and distillate tanks. Except for ketoprofen, all the PhACs were found in DS at concentrations below 300 ng L^{-1} (Figure 13a), after 32 d of AnOMBR-MD operation. Ketoprofen concentration was almost 600 ng L^{-1} in the DS and 300 ng L^{-1} in distillate. Ricci et al. [32] already reported on the limitation of the AnOMBR-MD in removing ketoprofen, due to its low molar weight and reduced anaerobic biodegradation [47]. Furthermore, rejection of ketoprofen by the FO-MD module operated with $MgCl_2$ as DS was 93% after 8 h of operation, because of its hydrophilicity (log K_{ow} = 0.39) and affinity with the FO membrane [33]. Thus, the accumulation of ketoprofen in the ML, over long-time operation may have increased its passage through the FO and MD membranes, reducing R_{AnOMBR} and $R_{AnOMBR\text{-}MD}$ to 75 and 87% (Figure 13b), respectively. Fluconazole, despite being hydrophilic (log K_{ow} = 0.56), due to size exclusion (molar mass of 360.83 g mol^{-1}), had R_{AnOMBR} of 97% and $R_{AnOMBR\text{-}MD}$ of 98.5%.

The system presented R_{AnOMBR} of more than 87% and $R_{AnOMBR\text{-}MD}$ higher than 95% for hydrophobic compounds, with log K_{ow} > 3 (17α-ethinylestradiol, fenofibrate and loratadine), Hydrophobicity reduced the interaction between the PhACs and the FO membrane, increasing the membrane rejection. Also, these three PhACs may have been removed by biotic and abiotic mechanisms during anaerobic biological treatment, contributing to the overall performance of the system [47]. It is worth emphasizing that for 17α-ethinylestradiol the removals were calculated considering the limit of detection, so, R_{AnOMBR} and $R_{AnOMBR\text{-}MD}$ could be higher than the reported values.

Betamethasone and prednisone have similar log K_{ow} values (1.68 and 1.66, respectively), however, a slight difference in their removal was observed. For betamethasone, R_{AnOMBR} was 90.2% and $R_{AnOMBR\text{-}MD}$ was 95.6%, while prednisone removal was 96.8% by the R_{AnOMBR} and 98% by the $R_{AnOMBR\text{-}MD}$. As shown by Faria et al. [47], under anaerobic conditions, betamethasone is mainly removed by biotic process and prednisone is removed by abiotic mechanisms, such as biosorption onto the sludge. With salinity build-up observed in the AnOMBR-MD, it is expected that the compounds removed through biotic process would be accumulated in the ML, which could justify the lower removal of betamethasone, compared to prednisone.

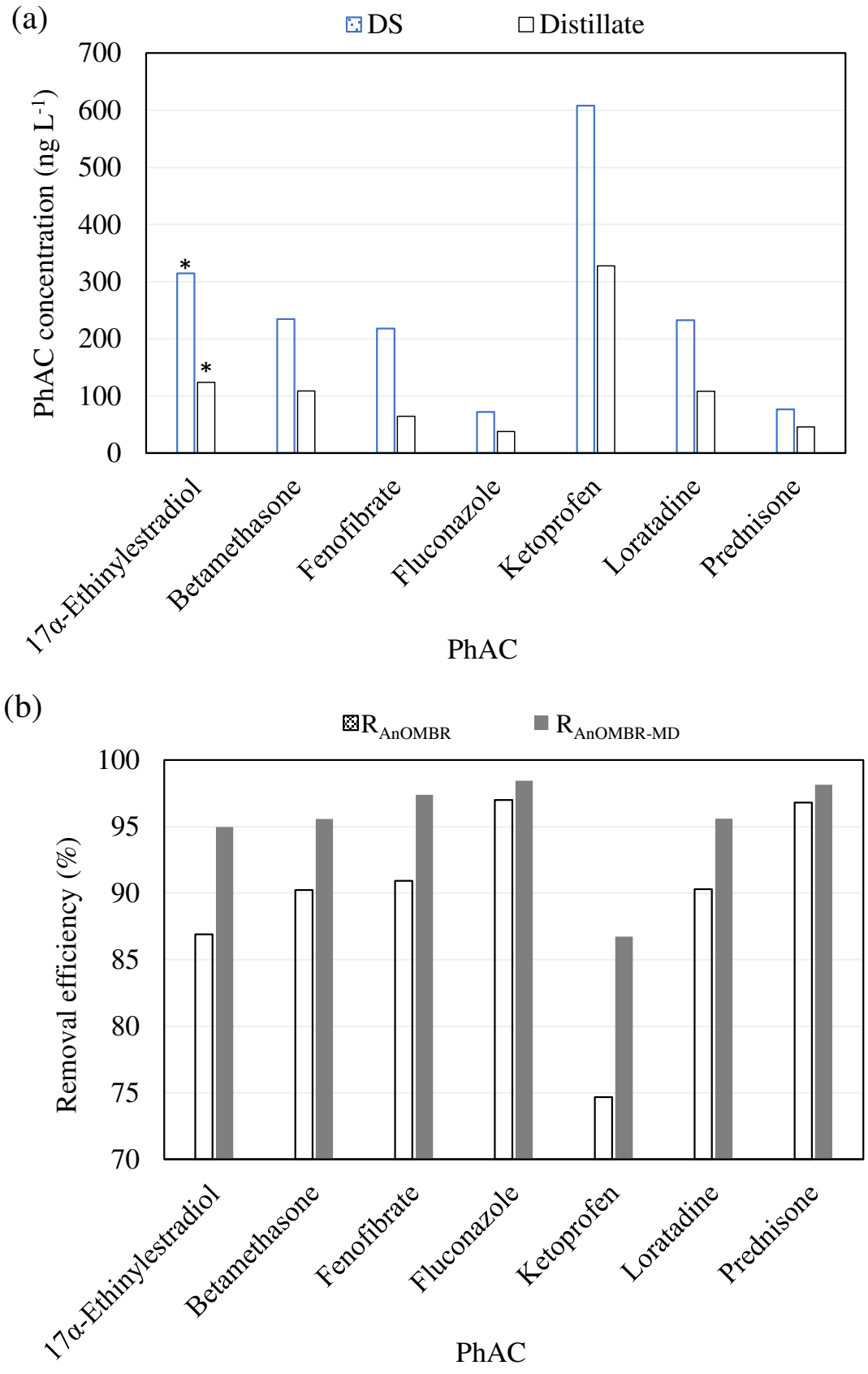


Figure 13 – (a) PhACs concentration and (b) removal efficiency in the AnOMBR-MD. (Feed solution concentration: 2000 ng L^{-1}). *limit of detection for 17α-ethinylestradiol.

The estrogenic activity of the synthetic wastewater spiked with 2 μg L^{-1}, used as feed solution, was 477 ng L^{-1} E2-eq. The ML presented lower estrogenicity than FS in all five samples collected during the AnOMBR-MD operation and the calculated biological removal (R_{Bio}) was higher than 65% (Figure 14b). The biological removal of estrogenic compounds was governed mainly by biodegradation (R_{biodeg}), which started at 64.1%, increasing to 90.1% in 11 days. Then, a significant decrease to 43.5% was observed on day 15, probably due to the effect of salinity build-up. After salinity stabilization, on day 22, R_{biodeg} returned to its initial value, which was maintained until the end of operation. Some studies have reported that anaerobic biodegradation of 17α-ethinylestradiol is difficult under high salinity and its removal is mainly due to abiotic mechanisms, like adsorption [47,89]. Nevertheless, the maximum removal by sorption onto the sludge ($R_{biosorp}$) was 27.6%, after 32 days of operation. These results indicate an adaptation of the microorganisms to the new operating conditions and metabolism of estrogenic compounds present in the reactor, resulting in reduction in estrogenic activity from the ML was observed at the end of the operation.

DS concentrations were always below 1.1 ng L^{-1} E2-eq (Figure 14a), due to the high rejection by the FO membrane combined with biological removal (> 99.9%) (Figure 14b). The overall removal efficiency of the system varied from 99.97 to > 99.99%, and 0.14 ng L^{-1} E2-eq was the maximum estrogenic activity detected in the distillate. Since 17α-ethinylestradiol has estrogenic activity close to 17β-estradiol [52], the concentration of 17α-ethinylestradiol in the distillate may be approximately 0.14 ng L^{-1}, indicating a higher removal for this PhAC, without considering the limit of detection in the LC-MS method. Ricci et al. [32] and Arcanjo et al. [52] observed that the AnOMBR-MD is very effective in removing micropollutants and estrogenic activity. In the present study, it was possible to confirm the high reduction in the estrogenic effect of these biologically active compounds, even with the PhACs concentration found in the distillate.

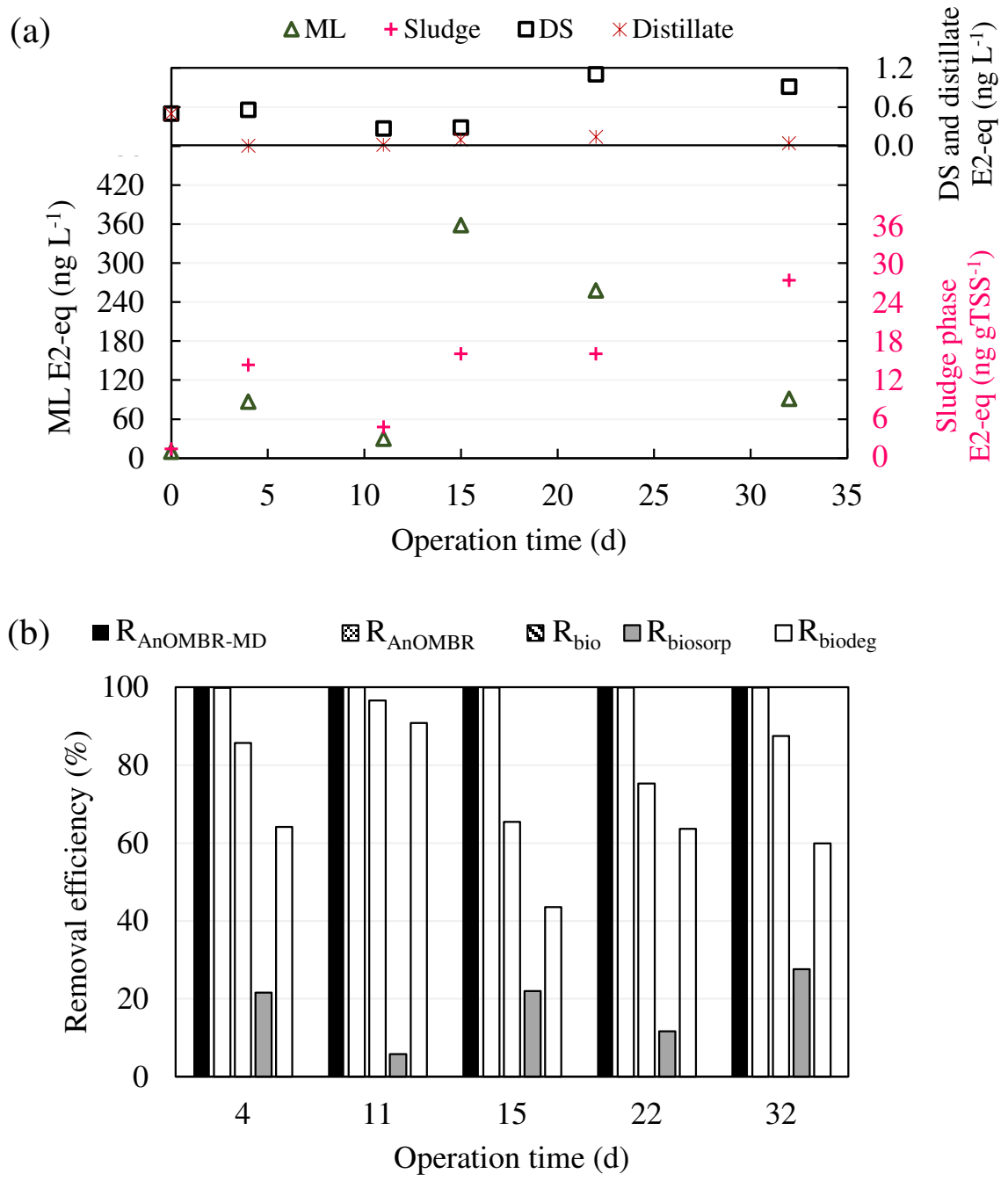


Figure 14 - (a) Estrogenic activity and (b) removal efficiency in the AnOMBR-MD. (FS estrogenic activity: 477 ng L^{-1} E2-eq).

3.6 Environmental and human health risk assessment

The AnOMBR-MD was efficient in removing PhACs and estrogenic activity and this was evident in the reduction of environmental and human health risks (Figure 15a). Nevertheless, a high acute environmental risk was verified in the distillate for ketoprofen and loratadine, due to the high concentration of ketoprofen and the higher toxicity of loratadine. Therefore, strategies to improve the removal of these compounds must be investigated, such as

the treatment of the DS, to avoid PhACs accumulation and reduce their passage through the MD membrane [90]. A high human risk for 17α-ethinylestradiol was also observed, because of its high limit of detection. With the combined investigation of PhACs concentration and the YES assay, it was possible to confirm a low risk of 17α-ethinylestradiol since its concentration was estimated to be 0.14 ng L^{-1}.

From the temporal analysis of the estrogenic activity in the distillate (Figure S5, supplementary material), the acute (RQac) and chronic (RQch) environmental risks related to the estrogenic activity were considered medium for the distillate at the beginning of operation (Figure S5a, supplementary material), after 4 d, risks were negligible, and then low until the end of the AnOMBR-MD operation. The same was verified for the human health risk (HQ). In a previous work [52], HQ and RQ were considered high, after the AnOMBR-MD system, due to the high detection limit of the YES assay. With the lower detection limit established in the present work, it was possible to verify the actual risk reduction ability of the AnOMBR-MD.

The Institute of Environment and Health [91] assessed several estrogenically-active chemicals present in the environment. It concluded that even drinking water that contains the worst-case level predicted for each of these compounds does not constitute a significant risk to human health when considered in terms of equivalence to the consumption of the natural hormone estradiol. However, the analysis did not take into consideration the effect of the mixture of these compounds. In any case, the risk evaluation of EDCs and their combined effect on human health is of great importance, so that any chance of potential risk may be predicted. Thus, the hybrid AnOMBR-MD demonstrated strong performance in reducing risks, even when human health is considered.

The ILCR of the feed solution with regard to estrogenic activity was considered unacceptable but this risk was reduced to negligible in distillate from the AnOMBR-MD (Figure S5b, supplementary material), as shown in Figure b. The assessment of cancer risk is of great relevance since epidemiological evidence continues to reveal the relationship between exposure to EDCs and carcinogenesis, although there are still some gaps in these studies [92]. Williams and Darbre [93] tested human breast cell exposure to some EDCs and observed that these compounds are directly related, even at low daily doses, to the proliferation of cancer. The unacceptable risk of the feed solution reinforces the importance of wastewater and water treatment plants in removing EDCs.

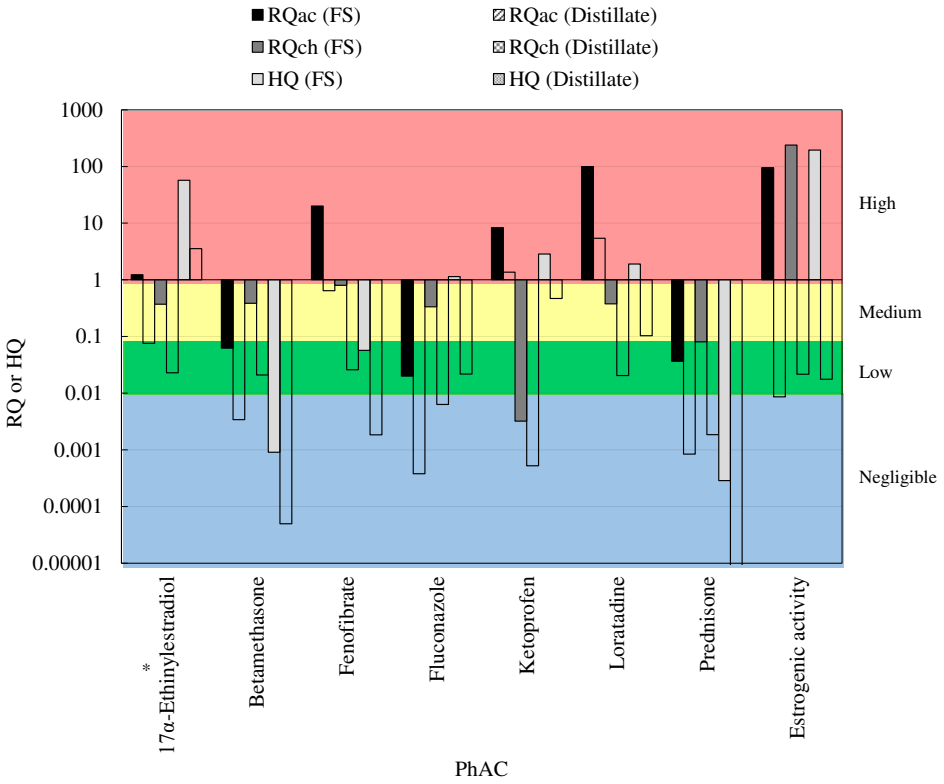


Figure 15 - Environmental and human health risks for AnOMBR-MD feed solution (FS) and distillate. RQac: acute environmental risk; RQch: chronic environmental risk; and HQ: human health risk. * Risk was calculated considering the limit of detection for 17α-ethinylestradiol.

4 Conclusion

The use of $MgCl_2$ as draw solute reduced the reverse salt flux and reduced salinity impacts on the microbial community of the AnOMBR-MD. Magnesite, monetite and struvite may have precipitated in the bioreactor, due to the accumulation of $P\text{-}PO_4^{3-}$ and $N\text{-}NH_4^+$ in the mixed liquor, combined with the increase in Mg^{2+} concentration from the reverse salt flux. The overall removal of PhACs was higher than 95%, except for ketoprofen (87%). Biological removal of estrogenic compounds was affected by the rapid salinity build-up in the bioreactor, but after conductivity stabilization, biosorption and biodegradation increased again. The AnOMBR-MD has great potential in treating municipal wastewaters containing endocrine disrupting compounds, reaching estrogenic compounds removals of greater than 99.99%, after 32 days.

Risk assessment showed that better removal of ketoprofen and loratadine is needed, since their presence led to high acute environmental risk of the distillate. Nevertheless, for

estrogenic activity, the AnOMBR-MD reduced environmental and non-carcinogenic human risks from high to low, while incremental lifetime carcinogenic risk decreased to negligible.

References

[1] WHO, WHO | State of the science of endocrine disrupting chemicals - 2012, (2012). http://www.who.int/ceh/publications/endocrine/en/ (accessed August 19, 2017).

[2] M. Gea, A. Toso, T. Schilirò, Estrogenic activity of biological samples as a biomarker, Science of The Total Environment. 740 (2020) 140050. https://doi.org/10.1016/j.scitotenv.2020.140050.

[3] P.Y. Kunz, C. Kienle, M. Carere, N. Homazava, R. Kase, In vitro bioassays to screen for endocrine active pharmaceuticals in surface and waste waters, Journal of Pharmaceutical and Biomedical Analysis. 106 (2015) 107–115. https://doi.org/10.1016/j.jpba.2014.11.018.

[4] T. aus der Beek, F.-A. Weber, A. Bergmann, S. Hickmann, I. Ebert, A. Hein, A. Küster, Pharmaceuticals in the environment-Global occurrences and perspectives: Pharmaceuticals in the global environment, Environ Toxicol Chem. 35 (2016) 823–835. https://doi.org/10.1002/etc.3339.

[5] C.G. Daughton, T.A. Ternes, Pharmaceuticals and personal care products in the environment: agents of subtle change?, Environmental Health Perspectives. 107 (1999) 32.

[6] G. Kaushik, M.A. Thomas, The potential association of psychoactive pharmaceuticals in the environment with human neurological disorders, Sustainable Chemistry and Pharmacy. 13 (2019) 100148. https://doi.org/10.1016/j.scp.2019.100148.

[7] E.O. Reis, A.F.S. Foureaux, J.S. Rodrigues, V.R. Moreira, Y.A.R. Lebron, L.V.S. Santos, M.C.S. Amaral, L.C. Lange, Occurrence, removal and seasonal variation of pharmaceuticals in Brasilian drinking water treatment plants, Environmental Pollution. 250 (2019) 773–781. https://doi.org/10.1016/j.envpol.2019.04.102.

[8] B. Roig, Pharmaceuticals in the Environment, IWA Publishing, 2010.

[9] A.V. Santos, C.F. Couto, Y.A. Lebron, V.R. Moreira, A.F.S. Foureaux, E.O. Reis, L.V. de Souza Santos, L.H. de Andrade, M.C.S. Amaral, L.C. Lange, Occurrence and risk assessment of pharmaceutically active compounds in water supply systems in Brazil, Science of The Total Environment. (2020) 141011. https://doi.org/10.1016/j.scitotenv.2020.141011.

[10] N.G.F.M. van der Aa, G.J. Kommer, J.E. van Montfoort, J.F.M. Versteegh, Demographic projections of future pharmaceutical consumption in the Netherlands, Water Science and Technology. 63 (2011) 825–831. https://doi.org/10.2166/wst.2011.120.

[11] S. Esplugas, D.M. Bila, L.G.T. Krause, M. Dezotti, Ozonation and advanced oxidation technologies to remove endocrine disrupting chemicals (EDCs) and pharmaceuticals and personal care products (PPCPs) in water effluents, Journal of Hazardous Materials. 149 (2007) 631–642. https://doi.org/10.1016/j.jhazmat.2007.07.073.

[12] E.R. Kabir, M.S. Rahman, I. Rahman, A review on endocrine disruptors and their possible impacts on human health, Environmental Toxicology and Pharmacology. 40 (2015) 241–258. https://doi.org/10.1016/j.etap.2015.06.009.

[13] F.D.L. Leusch, C. de Jager, Y. Levi, R. Lim, L. Puijker, F. Sacher, L.A. Tremblay, V.S. Wilson, H.F. Chapman, Comparison of Five in Vitro Bioassays to Measure Estrogenic Activity in Environmental Waters, Environmental Science & Technology. 44 (2010) 3853–3860. https://doi.org/10.1021/es903899d.

[14] B.I. Escher, M. Allinson, R. Altenburger, P.A. Bain, P. Balaguer, W. Busch, J. Crago, N.D. Denslow, E. Dopp, K. Hilscherova, A.R. Humpage, A. Kumar, M. Grimaldi, B.S. Jayasinghe, B. Jarosova, A. Jia, S. Makarov, K.A. Maruya, A. Medvedev, A.C. Mehinto, J.E. Mendez, A. Poulsen, E. Prochazka, J. Richard, A. Schifferli, D. Schlenk, S. Scholz, F. Shiraishi, S. Snyder, G. Su, J.Y.M. Tang, B. van der Burg, S.C. van der Linden, I. Werner, S.D. Westerheide, C.K.C. Wong, M. Yang, B.H.Y. Yeung, X. Zhang, F.D.L. Leusch, Benchmarking Organic Micropollutants in Wastewater, Recycled Water and Drinking Water with In Vitro Bioassays, Environ. Sci. Technol. 48 (2014) 1940–1956. https://doi.org/10.1021/es403899t.

[15] C. Pesci Pereira, T. da Conceição Pereira, G. Gomes, B.R. Quintaes, D.M. Bila, J.C. Campos, Evaluation of reduction estrogenic activity in the combined treatment of landfill leachate and sanitary sewage, Waste Management. 80 (2018) 339–348. https://doi.org/10.1016/j.wasman.2018.09.018.

[16] M. Kuzmanović, A. Ginebreda, M. Petrović, D. Barceló, Risk assessment based prioritization of 200 organic micropollutants in 4 Iberian rivers, Science of The Total Environment. 503–504 (2015) 289–299. https://doi.org/10.1016/j.scitotenv.2014.06.056.

[17] S.F. de Aquino, E.M.F. Brandt, C.A. de L. Chernicharo, Remoção de fármacos e desreguladores endócrinos em estações de tratamento de esgoto: revisão da literatura, Engenharia Sanitária e Ambiental. 18 (2013) 187–204. https://doi.org/10.1590/S1413-41522013000300002.

[18] C.F. Couto, L.C. Lange, M.C.S. Amaral, A critical review on membrane separation processes applied to remove pharmaceutically active compounds from water and wastewater, Journal of Water Process Engineering. 26 (2018) 156–175. https://doi.org/10.1016/j.jwpe.2018.10.010.

[19] A. Jelic, M. Gros, A. Ginebreda, R. Cespedes-Sánchez, F. Ventura, M. Petrovic, D. Barcelo, Occurrence, partition and removal of pharmaceuticals in sewage water and sludge during wastewater treatment, Water Research. 45 (2011) 1165–1176. https://doi.org/10.1016/j.watres.2010.11.010.

[20] X. Yang, R.C. Flowers, H.S. Weinberg, P.C. Singer, Occurrence and removal of pharmaceuticals and personal care products (PPCPs) in an advanced wastewater reclamation plant, Water Research. 45 (2011) 5218–5228. https://doi.org/10.1016/j.watres.2011.07.026.

[21] S.K. Maeng, B.G. Choi, K.T. Lee, K.G. Song, Influences of solid retention time, nitrification and microbial activity on the attenuation of pharmaceuticals and estrogens in membrane bioreactors, Water Research. 47 (2013) 3151–3162. https://doi.org/10.1016/j.watres.2013.03.014.

[22] F. Meng, S.-R. Chae, A. Drews, M. Kraume, H.-S. Shin, F. Yang, Recent advances in membrane bioreactors (MBRs): Membrane fouling and membrane material, Water Research. 43 (2009) 1489–1512. https://doi.org/10.1016/j.watres.2008.12.044.

[23] A. Achilli, T.Y. Cath, E.A. Marchand, A.E. Childress, The forward osmosis membrane bioreactor: A low fouling alternative to MBR processes, Desalination. 239 (2009) 10–21. https://doi.org/10.1016/j.desal.2008.02.022.

[24] M. Xie, W. Luo, H. Guo, L.D. Nghiem, C.Y. Tang, S.R. Gray, Trace organic contaminant rejection by aquaporin forward osmosis membrane: Transport mechanisms and membrane stability, Water Research. 132 (2018) 90–98. https://doi.org/10.1016/j.watres.2017.12.072.

[25] M. Yao, L. Duan, J. Wei, F. Qian, S.W. Hermanowicz, Carbamazepine removal from wastewater and the degradation mechanism in a submerged forward osmotic membrane bioreactor, Bioresource Technology. 314 (2020) 123732. https://doi.org/10.1016/j.biortech.2020.123732.

[26] A.M. Awad, R. Jalab, J. Minier-Matar, S. Adham, M.S. Nasser, S.J. Judd, The status of forward osmosis technology implementation, Desalination. 461 (2019) 10–21. https://doi.org/10.1016/j.desal.2019.03.013.

[27] X. Wang, H. Wang, M. Xie, Secret underneath: Fouling of membrane support layer in anaerobic osmotic membrane bioreactor (AnOMBR), Journal of Membrane Science. 614 (2020) 118530. https://doi.org/10.1016/j.memsci.2020.118530.

[28] X. Wang, C. Wang, C.Y. Tang, T. Hu, X. Li, Y. Ren, Development of a novel anaerobic membrane bioreactor simultaneously integrating microfiltration and forward osmosis membranes for low-strength wastewater treatment, Journal of Membrane Science. 527 (2017) 1–7. https://doi.org/10.1016/j.memsci.2016.12.062.

[29] H. Luo, Q. Wang, T.C. Zhang, T. Tao, A. Zhou, L. Chen, X. Bie, A review on the recovery methods of draw solutes in forward osmosis, Journal of Water Process Engineering. 4 (2014) 212–223. https://doi.org/10.1016/j.jwpe.2014.10.006.

[30] N.C. Nguyen, S.-S. Chen, H.T. Nguyen, S.S. Ray, H.H. Ngo, W. Guo, P.-H. Lin, Innovative sponge-based moving bed–osmotic membrane bioreactor hybrid system using a new class of draw solution for municipal wastewater treatment, Water Research. 91 (2016) 305–313. https://doi.org/10.1016/j.watres.2016.01.024.

[31] P. Wang, T.-S. Chung, Recent advances in membrane distillation processes: Membrane development, configuration design and application exploring, Journal of Membrane Science. 474 (2015) 39–56. https://doi.org/10.1016/j.memsci.2014.09.016.

[32] B.C. Ricci, G.S. Arcanjo, V.R. Moreira, Y.A.R. Lebron, K. Koch, F.C.R. Costa, B.P. Ferreira, F.C. Lisboa, L.D. Miranda, C.V. de Faria, L.C. Lange, M. Amaral, A novel submerged anaerobic osmotic membrane bioreactor coupled to membrane distillation for water reclamation from municipal wastewater, Chemical Engineering Journal. (2021) 128645. https://doi.org/10.1016/j.cej.2021.128645.

[33] G.S. Arcanjo, F.C.R. Costa, B.C. Ricci, A.H. Mounteer, E.N.M.L. de Melo, B.F. Cavalcante, A.V. Araújo, C.V. Faria, M.C.S. Amaral, Draw solution solute selection for a

hybrid forward osmosis-membrane distillation module: Effects on trace organic compound rejection, water flux and polarization, Chemical Engineering Journal. 400 (2020) 125857. https://doi.org/10.1016/j.cej.2020.125857.

[34] K. Yetilmezsoy, F. Ilhan, E. Kocak, H.M. Akbin, Feasibility of struvite recovery process for fertilizer industry: A study of financial and economic analysis, Journal of Cleaner Production. 152 (2017) 88–102. https://doi.org/10.1016/j.jclepro.2017.03.106.

[35] G. Qiu, Y.-P. Ting, Direct phosphorus recovery from municipal wastewater via osmotic membrane bioreactor (OMBR) for wastewater treatment, Bioresource Technology. 170 (2014) 221–229. https://doi.org/10.1016/j.biortech.2014.07.103.

[36] H.-M. Chang, S.-S. Chen, N.C. Nguyen, W.-S. Chang, S. Sinha Ray, Osmosis membrane bioreactor–microfiltration with magnesium-based draw solute for salinity reduction and phosphorus recovery, International Biodeterioration & Biodegradation. 124 (2017) 169–175. https://doi.org/10.1016/j.ibiod.2017.05.022.

[37] S.J. Khan, M.S. Siddique, H.M.A. Shahzad, Performance evaluation of hybrid OMBR-MD using organic and inorganic draw solutions, Water Science and Technology. 78 (2018) 776–785. https://doi.org/10.2166/wst.2018.345.

[38] G. Mockaitis, J.L.R. Pantoja, J.A.D. Rodrigues, E. Foresti, M. Zaiat, Continuous anaerobic bioreactor with a fixed-structure bed (ABFSB) for wastewater treatment with low solids and low applied organic loading content, Bioprocess Biosyst Eng. 37 (2014) 1361–1368. https://doi.org/10.1007/s00449-013-1108-y.

[39] B.C. Ricci, B. Skibinski, K. Koch, C. Mancel, C.Q. Celestino, I.L.C. Cunha, M.R. Silva, C.B. Alvim, C.V. Faria, L.H. Andrade, L.C. Lange, M.C.S. Amaral, Critical performance assessment of a submerged hybrid forward osmosis - membrane distillation system, Desalination. 468 (2019) 114082. https://doi.org/10.1016/j.desal.2019.114082.

[40] APHA, Standard Methods for the Examination of Water and Wastewater, 23rd ed., APHA, AWWA, WPCF, New York, 2017.

[41] H. Kapp, Schlammfaulung mit hohem Feststoffgehalt, Kommissionsverlag Oldenbourg, 1984. http://agris.fao.org/agris-search/search.do?recordID=US201300384705 (accessed February 4, 2020).

[42] V.T. Mota, F.S. Santos, T.A. Araújo, M.C.S. Amaral, Evaluation of titration methods for volatile fatty acids measurement: effect of the bicarbonate interference and feasibility for the monitoring of anaerobic reactors, Water Practice and Technology. 10 (2015) 486–495. https://doi.org/10.2166/wpt.2015.056.

[43] Michel. DuBois, K.A. Gilles, J.K. Hamilton, P.A. Rebers, Fred. Smith, Colorimetric Method for Determination of Sugars and Related Substances, Anal. Chem. 28 (1956) 350–356. https://doi.org/10.1021/ac60111a017.

[44] O.H. Lowry, N.J. Rosebrough, A.L. Farr, R.J. Randall, Protein measurement with the Folin phenol reagent., Journal of Biological Chemistry. 193 (1951) 265–275.

[45] D.-Q. He, Y.-J. Zhang, C.-S. He, H.-Q. Yu, Changing profiles of bound water content and distribution in the activated sludge treatment by NaCl addition and pH modification, Chemosphere. 186 (2017) 702–708. https://doi.org/10.1016/j.chemosphere.2017.08.045.

[46] L. Zheng, D. Yu, G. Wang, Z. Yue, C. Zhang, Y. Wang, J. Zhang, J. Wang, G. Liang, Y. Wei, Characteristics and formation mechanism of membrane fouling in a full-scale RO wastewater reclamation process: Membrane autopsy and fouling characterization, Journal of Membrane Science. 563 (2018) 843–856. https://doi.org/10.1016/j.memsci.2018.06.043.

[47] C.V. Faria, B.C. Ricci, A.F.R. Silva, M.C.S. Amaral, F.V. Fonseca, Removal of micropollutants in domestic wastewater by expanded granular sludge bed membrane bioreactor, Process Safety and Environmental Protection. 136 (2020) 223–233. https://doi.org/10.1016/j.psep.2020.01.033.

[48] M.T.L. do Nascimento, A.D. de O. Santos, L.C. Felix, G. Gomes, M. de Oliveira e Sá, D.L. da Cunha, N. Vieira, R.A. Hauser-Davis, J.A. Baptista Neto, D.M. Bila, Determination of water quality, toxicity and estrogenic activity in a nearshore marine environment in Rio de Janeiro, Southeastern Brazil, Ecotoxicology and Environmental Safety. 149 (2018) 197–202. https://doi.org/10.1016/j.ecoenv.2017.11.045.

[49] J. Martín, J.L. Santos, I. Aparicio, E. Alonso, Multi-residue method for the analysis of pharmaceutical compounds in sewage sludge, compost and sediments by sonication-assisted extraction and LC determination: Liquid Chromatography, J. Sep. Science. 33 (2010) 1760–1766. https://doi.org/10.1002/jssc.200900873.

[50] E.J. Routledge, J.P. Sumpter, Estrogenic activity of surfactants and some of their degradation products assessed using a recombinant yeast screen, Environmental Toxicology and Chemistry. 15 (1996) 241–248.

[51] D. Bila, A.F. Montalvão, D. de A. Azevedo, M. Dezotti, Estrogenic activity removal of 17β-estradiol by ozonation and identification of by-products, Chemosphere. 69 (2007) 736–746. https://doi.org/10.1016/j.chemosphere.2007.05.016.

[52] G.S. Arcanjo, B.C. Ricci, C.R. dos Santos, F.C.R. Costa, U.C.M. Silva, A.H. Mounteer, K. Koch, P.R. da Silva, V.L. Santos, M.C.S. Amaral, Effective removal of pharmaceutical compounds and estrogenic activity by a hybrid anaerobic osmotic membrane bioreactor – Membrane distillation system treating municipal sewage, Chemical Engineering Journal. 416 (2021) 129151. https://doi.org/10.1016/j.cej.2021.129151.

[53] W.A. Phillip, J.S. Yong, M. Elimelech, Reverse Draw Solute Permeation in Forward Osmosis: Modeling and Experiments, Environ. Sci. Technol. 44 (2010) 5170–5176. https://doi.org/10.1021/es100901n.

[54] C.Y. Tang, Q. She, W.C.L. Lay, R. Wang, A.G. Fane, Coupled effects of internal concentration polarization and fouling on flux behavior of forward osmosis membranes during humic acid filtration, Journal of Membrane Science. 354 (2010) 123–133. https://doi.org/10.1016/j.memsci.2010.02.059.

[55] G. Qiu, H. Chen, D.S. Srinivasa Raghavan, Y.-P. Ting, Removal behaviors of antibiotics in a hybrid microfiltration-forward osmotic membrane bioreactor for real municipal wastewater treatment, Chemical Engineering Journal. (2021) 129146. https://doi.org/10.1016/j.cej.2021.129146.

[56] D. Crutchik, A. Sánchez, J.M. Garrido, Simulation and experimental validation of multiple phosphate precipitates in a saline industrial wastewater, Separation and Purification Technology. 118 (2013) 81–88. https://doi.org/10.1016/j.seppur.2013.06.041.

[57] G. Jia, H. Zhang, J. Krampe, T. Muster, B. Gao, N. Zhu, B. Jin, Applying a chemical equilibrium model for optimizing struvite precipitation for ammonium recovery from anaerobic digester effluent, Journal of Cleaner Production. 147 (2017) 297–305. https://doi.org/10.1016/j.jclepro.2017.01.116.

[58] D.J. Caldwell, F. Mastrocco, E. Nowak, J. Johnston, H. Yekel, D. Pfeiffer, M. Hoyt, B.M. DuPlessie, P.D. Anderson, An Assessment of Potential Exposure and Risk from Estrogens in Drinking Water, Environmental Health Perspectives. 118 (2010) 338–344. https://doi.org/10.1289/ehp.0900654.

[59] A. Wenzel, J. Müller, T. Ternes, Study on endocrine disrupters in drinking water, Schmallenberg and Wiesbaden, Germany, 2003.

[60] California EPA, Expedited Cancer Potency Values and Proposed Regulatory levels for certain proposition 65 carcinogens (Reproductive and cancer hazard assessment section), (1992). https://oehha.ca.gov/media/downloads/proposition-65/report/expcancer.pdf.

[61] M. Molina-Muñoz, J.M. Poyatos, R. Vílchez, E. Hontoria, B. Rodelas, J. González-López, Effect of the concentration of suspended solids on the enzymatic activities and biodiversity of a submerged membrane bioreactor for aerobic treatment of domestic wastewater, Appl Microbiol Biotechnol. 73 (2007) 1441–1451. https://doi.org/10.1007/s00253-006-0594-0.

[62] V. Parida, H.Y. Ng, Forward osmosis organic fouling: Effects of organic loading, calcium and membrane orientation, Desalination. 312 (2013) 88–98. https://doi.org/10.1016/j.desal.2012.04.029.

[63] L. Chen, Y. Gu, C. Cao, J. Zhang, J.-W. Ng, C. Tang, Performance of a submerged anaerobic membrane bioreactor with forward osmosis membrane for low-strength wastewater treatment, Water Research. 50 (2014) 114–123. https://doi.org/10.1016/j.watres.2013.12.009.

[64] Y. Gu, L. Chen, J.-W. Ng, C. Lee, V.W.-C. Chang, C.Y. Tang, Development of anaerobic osmotic membrane bioreactor for low-strength wastewater treatment at mesophilic condition, Journal of Membrane Science. 490 (2015) 197–208. https://doi.org/10.1016/j.memsci.2015.04.032.

[65] A. Achilli, T.Y. Cath, A.E. Childress, Selection of inorganic-based draw solutions for forward osmosis applications, Journal of Membrane Science. 364 (2010) 233–241. https://doi.org/10.1016/j.memsci.2010.08.010.

[66] L. Martínez-Díez, M.I. Vázquez-González, Temperature and concentration polarization in membrane distillation of aqueous salt solutions, Journal of Membrane Science. 156 (1999) 265–273. https://doi.org/10.1016/S0376-7388(98)00349-4.

[67] X. Song, M. Xie, Y. Li, G. Li, W. Luo, Salinity build-up in osmotic membrane bioreactors: Causes, impacts, and potential cures, Bioresource Technology. 257 (2018) 301–310. https://doi.org/10.1016/j.biortech.2018.02.101.

[68] J.D. Muñoz Sierra, M.J. Oosterkamp, W. Wang, H. Spanjers, J.B. van Lier, Impact of long-term salinity exposure in anaerobic membrane bioreactors treating phenolic wastewater: Performance robustness and endured microbial community, Water Research. 141 (2018) 172–184. https://doi.org/10.1016/j.watres.2018.05.006.

[69] F.I. Hai, K. Yamamoto, Membrane Biological Reactors, in: Treatise on Water Science, Elsevier, 2011: pp. 571–613. https://doi.org/10.1016/B978-0-444-53199-5.00096-8.

[70] W. Luo, F.I. Hai, J. Kang, W.E. Price, W. Guo, H.H. Ngo, K. Yamamoto, L.D. Nghiem, Effects of salinity build-up on biomass characteristics and trace organic chemical removal: Implications on the development of high retention membrane bioreactors, Bioresource Technology. 177 (2015) 274–281. https://doi.org/10.1016/j.biortech.2014.11.084.

[71] M. Remy, H. Temmink, P. van den Brink, W. Rulkens, Low powdered activated carbon concentrations to improve MBR sludge filterability at high salinity and low temperature, Desalination. 276 (2011) 403–407. https://doi.org/10.1016/j.desal.2011.03.080.

[72] H. Zhang, Z. Gao, L. Zhang, L. Song, Performance enhancement and fouling mitigation by organic flocculant addition in membrane bioreactor at high salt shock, Bioresource Technology. 164 (2014) 34–40. https://doi.org/10.1016/j.biortech.2014.04.053.

[73] R. Valladares Linares, Z. Li, V. Yangali-Quintanilla, Q. Li, G. Amy, Cleaning protocol for a FO membrane fouled in wastewater reuse, Desalination and Water Treatment. 51 (2013) 4821–4824. https://doi.org/10.1080/19443994.2013.795345.

[74] P.B. Moser, G.R. dos Anjos Silva, L.S.F. Lima, V.R. Moreira, Y.A.R. Lebron, E.C. de Paula, M.C.S. Amaral, Effect of organic and inorganic draw solution on recalcitrant compounds build up in a hybrid ultrafiltration-osmotic membrane reactor treating refinery effluent, Chemical Engineering Journal. 403 (2021) 126374. https://doi.org/10.1016/j.cej.2020.126374.

[75] J.-J. Lay, Y.-Y. Li, T. Noike, Influences of pH and moisture content on the methane production in high-solids sludge digestion, Water Research. 31 (1997) 1518–1524. https://doi.org/10.1016/S0043-1354(96)00413-7.

[76] A. Silva-Teira, J.R. Vázquez-Padín, R. Weiler, R. Fernández-González, F. Rogalla, J.M. Garrido, Performance of a hybrid membrane bioreactor treating a low strength and alkalinity wastewater, Process Biochemistry. 66 (2018) 176–182. https://doi.org/10.1016/j.procbio.2017.12.015.

[77] J. Zhou, R. Zhang, F. Liu, X. Yong, X. Wu, T. Zheng, M. Jiang, H. Jia, Biogas production and microbial community shift through neutral pH control during the anaerobic digestion of pig manure, Bioresource Technology. 217 (2016) 44–49. https://doi.org/10.1016/j.biortech.2016.02.077.

[78] G. Wang, D. Wang, L. Huang, Y. Song, Z. Chen, M. Du, Enhanced production of volatile fatty acids by adding a kind of sulfate reducing bacteria under alkaline pH, Colloids and Surfaces B: Biointerfaces. 195 (2020) 111249. https://doi.org/10.1016/j.colsurfb.2020.111249.

[79] L. Feng, Y. Li, C. Chen, X. Liu, X. Xiao, X. Ma, R. Zhang, Y. He, G. Liu, Biochemical Methane Potential (BMP) of Vinegar Residue and the Influence of Feed to

Inoculum Ratios on Biogas Production, BioResources. 8 (2013) 2487–2498. https://doi.org/10.15376/biores.8.2.2487-2498.

[80] D.A. Stafford, The effects of mixing and volatile fatty acid concentrations on anaerobic digester performance, Biomass. 2 (1982) 43–55. https://doi.org/10.1016/0144-4565(82)90006-3.

[81] M. Yao, Y.C. Woo, J. Ren, L.D. Tijing, J.-S. Choi, S.-H. Kim, H.K. Shon, Volatile fatty acids and biogas recovery using thermophilic anaerobic membrane distillation bioreactor for wastewater reclamation, Journal of Environmental Management. 231 (2019) 833–842. https://doi.org/10.1016/j.jenvman.2018.11.009.

[82] N. Cong Nguyen, H. Cong Duong, S.-S. Chen, H. Thi Nguyen, H. Hao Ngo, W. Guo, H. Quang Le, C. Cong Duong, L. Thuy Trang, A. Hoang Le, X. Thanh Bui, P. Dan Nguyen, Water and nutrient recovery by a novel moving sponge – Anaerobic osmotic membrane bioreactor – Membrane distillation (AnOMBR-MD) closed-loop system, Bioresource Technology. 312 (2020) 123573. https://doi.org/10.1016/j.biortech.2020.123573.

[83] T. Hu, X. Wang, C. Wang, X. Li, Y. Ren, Impacts of inorganic draw solutes on the performance of thin-film composite forward osmosis membrane in a microfiltration assisted anaerobic osmotic membrane bioreactor, RSC Advances. 7 (2017) 16057–16063. https://doi.org/10.1039/C7RA01524K.

[84] M. Darestani, V. Haigh, S.J. Couperthwaite, G.J. Millar, L.D. Nghiem, Hollow fibre membrane contactors for ammonia recovery: Current status and future developments, Journal of Environmental Chemical Engineering. 5 (2017) 1349–1359. https://doi.org/10.1016/j.jece.2017.02.016.

[85] B. Norddahl, V.G. Horn, M. Larsson, J.H. du Preez, K. Christensen, A membrane contactor for ammonia stripping, pilot scale experience and modeling, Desalination. 199 (2006) 172–174. https://doi.org/10.1016/j.desal.2006.03.037.

[86] R.W. Holloway, J. Regnery, L.D. Nghiem, T.Y. Cath, Removal of Trace Organic Chemicals and Performance of a Novel Hybrid Ultrafiltration-Osmotic Membrane Bioreactor, Environmental Science & Technology. 48 (2014) 10859–10868. https://doi.org/10.1021/es501051b.

[87] W. Luo, F.I. Hai, W.E. Price, W. Guo, H.H. Ngo, K. Yamamoto, L.D. Nghiem, Phosphorus and water recovery by a novel osmotic membrane bioreactor–reverse osmosis system, Bioresource Technology. 200 (2016) 297–304. https://doi.org/10.1016/j.biortech.2015.10.029.

[88] G. Qiu, Y.-M. Law, S. Das, Y.-P. Ting, Direct and Complete Phosphorus Recovery from Municipal Wastewater Using a Hybrid Microfiltration-Forward Osmosis Membrane Bioreactor Process with Seawater Brine as Draw Solution, Environmental Science & Technology. 49 (2015) 6156–6163. https://doi.org/10.1021/es504554f.

[89] G.-G. Ying, R.S. Kookana, Degradation of Five Selected Endocrine-Disrupting Chemicals in Seawater and Marine Sediment, Environ. Sci. Technol. 37 (2003) 1256–1260. https://doi.org/10.1021/es0262232.

[90] M. Xie, L.D. Nghiem, W.E. Price, M. Elimelech, A Forward Osmosis–Membrane Distillation Hybrid Process for Direct Sewer Mining: System Performance and Limitations, Environmental Science & Technology. 47 (2013) 13486–13493. https://doi.org/10.1021/es404056e.

[91] Institute of Environment and Health, A review of latest endocrine disrupting chemicals research implications for drinking water, (2012). http://dwi.gov.uk/research/completed-research/reports/DWI70_2_266.pdf.

[92] T.J. Houston, R. Ghosh, Untangling the association between environmental endocrine disruptive chemicals and the etiology of male genitourinary cancers, Biochemical Pharmacology. 172 (2020) 113743. https://doi.org/10.1016/j.bcp.2019.113743.

[93] G.P. Williams, P.D. Darbre, Low-dose environmental endocrine disruptors, increase aromatase activity, estradiol biosynthesis and cell proliferation in human breast cells, Molecular and Cellular Endocrinology. 486 (2019) 55–64. https://doi.org/10.1016/j.mce.2019.02.016.

3 General conclusion

The performance of an AnOMBR-MD treating municipal sewage was investigated. First, when NaCl was used to compose the DS, removal efficiencies of more than 97% of dissolved organic carbon and P-PO_4^{3-} were achieved. For N-NH_4^+, removal of 77.8% was observed, due to the accumulation of this nutrient in the anaerobic treatment. Permeate fluxes in FO and MD reduced almost 80%, because of ICP, ECP and J_s, that reduced the effective osmotic pressure difference, in FO, and temperature and concentration polarization in MD. Microbial community changed as a result of salinity build-up and the presence of pharmaceutical drugs. Nevertheless, since the system can completely reject the mixed liquor volatile suspended solids, microbial richness and diversity increased, with possible improvement on the overall removal of organic micropollutants and estrogenic activity.

$MgCl_2$ was selected as the best salt to be used as draw solute in a submerged FO-MD module, since the specific salt flux in the FO was the lowest one, among the 5 solutes investigated. Organic micropollutants rejection by FO was higher when J_s was low. Inorganic salts were completely rejected by the MD membrane. From the 7 pharmaceutical drugs evaluated, only ketoprofen was detected in the distillate, after 8 h of operation.

In the AnOMBR-MD operation with $MgCl_2$ as a draw solute, Js reduced and after 21 d the electrical conductivity in the ML stabilized. Even with the lower reduction in osmotic pressure difference, FO permeate flux reduced 82%, which indicates that other factors, such as ICP and ECP, must be predominant on FO. The influence of organic and inorganic contaminants accumulation in DS was also verified. Cristal deposition and pore blocking were observed in MD membrane, because of concentration polarization in the MD membrane surface. The removal of dissolved organic carbon was greater than 90%, but concentration of 13 mg L^{-1} was detected in distillate. The P-PO_4^{3-} concentration in the distillate and DS was always bellow the limit of detection. Due to the great rejection by the FO membrane, Mg^{2+}, P-PO_4^{3-} and N-NH_4^+ accumulation in the ML could led to struvite, magnesite and monetite precipitation in the ML.

Estrogenic activity removal by the AnOMBR-MD was not affected by the salt used in the DS, which shows the system capacity in retaining contaminants, even if the biological removal is compromised by the salinity build-up. The removal of pharmaceutical active compounds was higher than 95%, except for ketoprofen, with 87% removal, when $MgCl_2$ was used to compose DS. For NaCl as draw solute, removal was greater than 96.4%.

The system showed a remarkable potential in reducing environmental and human health risks. However, ketoprofen and loratadine still attributed high acute environmental risk to the distillate, in the operation with $MgCl_2$ as DS, because of the high concentration and the higher toxicity, respectively. So, it is necessary to improve the removal of micropollutants with more toxicity, to guarantee acceptable risks on the distillate.

Appendix A – Supplementary material chapter 1

Tables

Table S1 - Assessment factors to derive PNEC

Available data	Assessment factor
Long-term NOECs from at least three species (normally fish, daphnia and algae) representing three trophic levels	10
Two long-term NOECs from species representing two trophic levels (fish and/or daphnia and/or algae)	50
One long-term NOEC (either fish or daphnia)	100
At least one short-term L(E)C50 from each of three trophic levels of the base-set (fish, daphnia and algae)	1000

Source: European Commission [7].

Table S2 - PhACs E(L)C50 values

Pharmaceuticals	**Taxon**	**Specie**	**E(L)C50**	**Value (mg L^{-1})**	**Reference**
17α-Ethinylestradiol	Crustacean	*Daphnia similis*	EC50 (Mortality - 48 h)	1.63	[8]
Betamethasone	Algae	-	EC50 (ECOSAR)	41	[9]
	Crustacean	-	EC50 (ECOSAR)	32	[9]
	Fish	-	EC50 (ECOSAR)	37	[9]
Fenofibrate	Algae	-	EC50 (ECOSAR)	0.1	[9]
	Crustacean	*Ceriodaphnia dubia*	EC50 (Growth inhibition - 7d)	0.76	[10]
	Fish	*Poeciliopsis lucida*	EC50 (Cytotoxicity - 24h)	3.25	[11]
Fluconazole	Crustacean	*Thamnocephalus platyurus*	LC50 (Immobilization - 24h)	100	[12]
	Fish	*Oryzias latipes*	LC50 (Mortality - 96h)	100	[12]
Ketoprofen	Algae	*Pseudokirchneriella subcapitata*	EC50 (Mortality - 96 h)	0.24	[13]
	Fish	*Danio rerio*	LC50 (Mortality - 96h)	632	[14]
Loratadine	Algae	*Pseudokirchneriella subcapitata*	EC50 (Growth inhibition - 50%)	2.15	[15]
	Crustacean	*Ceriodaphnia dubia*	EC50 (Reproduction inhibition - 50%)	0.03	[15]
	Rotifer	*Brachionus calyciflorus*	EC50 (Reproduction inhibition - 50%)	0.05	[15]
	Fish	-	EC50 (ECOSAR)	0.02	[9]
Prednisone	Crustacean	*Brachionus calyciflorus*	LC50 (Mortality - 24h)	54.6	[16]
17β-estradiol				5×10^{-6}*	[17]

*PNEC value.

Table S3 - PhACs NOEC values

Pharmaceuticals	Taxon	Specie	NOEC	Value (mg L^{-1})	Reference
17α-Ethinylestradiol	Fish	*Fundulus heteroclitus*	NOEC (Mortality - 21 d)	0.5	[18]
	Crustacean	*Daphnia*	NOEC (Reproduction)	0.387	[19]
	Algae	-	-	0.054	[19]
Betamethasone	Algae	*Selenastrum capricornutum*	NOEC (growth rate and yield - 72 h)	34	[20]
	Crustacean	*Daphnia magna*	NOEC (parental survival - 21 d)	17	[20]
	Fish	*Pimephales promelas*	NOEC (mean dry weight - 32 d)	0.052	[20]
Fenofibrate	Algae	*Pseudokirchneriella subcapitata*	NOEC (Population growth rate - 3 d)	3.12	[10]
	Crustacean	*Ceriodaphnia dubia*	NOEC (Growth inhibition - 7 d)	0.039	[10]
	Fish	*Pimephales promelas*	NOEC (Morphology - 7 d)	0.025	[21]
Fluconazole	Algae	*Pseudokirchneriella subcapitata*	NOEC (Growth inhibition - 72 h)	3.06	[22]
	Aquatic plant	*Lemna minor*	NOEC (Growth rate - 7 d)	0.3	[23]
Ketoprofen	Algae	*Pseudokirchneriella subcapitata*	NOEC (Growth inhibition - 72 h)	9.94	[24]
	Crustacean	*Ceriodaphnia dubia*	NOEC (Reproduction - 6 to 8 d)	22.5	[24]
	Fish	*Danio rerio*	NOEC (Hatch, mortality, growth - 9 d)	6.25	[24]
Loratadine	Crustacean	*Daphnia magna*	NOEC (Reproduction - 21 d)	0.078	[25]
	Algae	*Pseudokirchneriella subcapitata*	NOEC (Growth inhibition - 72 h)	0.053	[25]
	Fish	*Pimephales promelas*	NOEC (Hatch, mortality, growth - 28 d)	0.084	[25]
Prednisone	Crustacean	-	NOEC (ECOSAR)	2.48	[26]
17β-estradiol				2×10^{-6}*	[17]

*PNEC value.

Table S4 - PhACs TDI and DWGL values

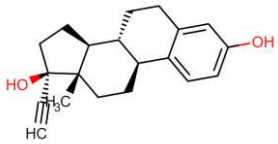
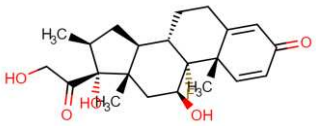
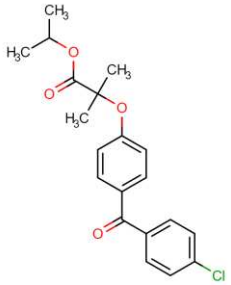
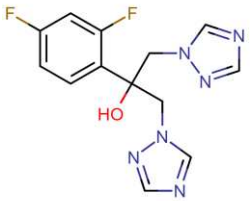
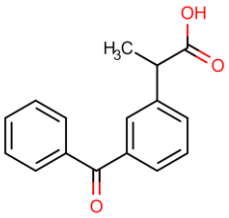
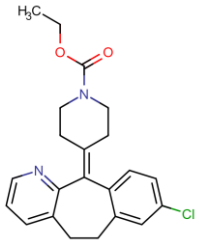
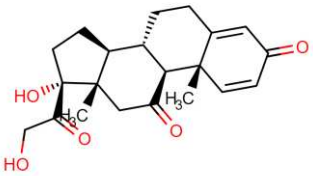
PhCs	TDI (µg kg^{-1} d^{-1})	Reference	DWGL (µg L^{-1})
17α-Ethynilestradiol	0.001	[27]	0.035
Betamethasone	63	[28]	2205
Fenofibrate	1	[29]	35
Fluconazole	0.05	[30]	1.75
Ketoprofen	0.02	[31]	0.7
Loratadine	0.03	[32]	1.05
Prednisone	200	[33]	7000
17β-estradiol (E2-eq.)	0.00007	[34]	0.00245

Table S5 - Parameters concentration in the bulk sludge in AnOMBR-MD operation

Parameter	Day 0 (Seed sludge)	Day 50
pH	7.9	8.1
Alkalinity (mg$CaCO_3$ L^{-1})	367.2	550.8
VFA (mgHAc L^{-1})	6.20	34.60
DOC (mg L^{-1})	19.10	58.34
N-NH_4^+ (mg L^{-1})	35.55	27.57
P-PO_4^{3-} (mg L^{-1})	6.00	31.69

Appendix B – Supplementary material chapter 2

Table S1 - Molecular structure of the selected pharmaceutical drugs used

Compound (Chemical Formula)	**Molecular Structure[a]**
17α-Ethynylestradiol ($C_{20}H_{24}O_2$)	
Betamethasone ($C_{22}H_{29}FO_5$)	
Fenofibrate ($C_{20}H_{21}ClO_4$)	
Fluconazole ($C_{13}H_{12}F_2N_6O$)	
Ketoprofen ($C_{16}H_{14}O_3$)	
Loratadine ($C_{22}H_{23}ClN_2O_2$)	
Prednisone ($C_{21}H_{26}O_5$)	

https://chemicalize.com/ developed by ChemAxon (http://www.chemaxon.com)

Table S2 - Draw solution parameters used to calculate permeate flux and polarizations in FO and MD processes

Solute	**T_F (°C)**	**T_{DS} (°C)**	**C_{DS} ($g.L^{-1}$)**	**ρ_{DS} ($kg.m^{-3}$)**	**A_{FO} (10^{-12} $m^3.m^{-2}.s^{-1}.Pa^{-1}$)**	**ϕ**	**μ_{oDS} (mPa.s)**	**μ_{DS} (mPa.s)**	**D_o (10^{-9} $m^2.s^{-1}$)**	**$k_{f.DS}$ ($W.m^{-1}.K^{-1}$)**	**$c_{p.DS}$ ($kJ.kg^{-1}.K^{-1}$)**	**$a_{w.DS}$**	**h_{DS} ($W.m^{-2}.K^{-1}$)**
NaCl	37.6	44.6	33.51	1013.96	3.21	0.32	0.94	0.64	1.47	0.60	4.03	0.98	351.14
$MgCl_2$	37.1	45.1	34.02	1017.81	3.24	0.18	1.01	0.67	1.05	0.60	3.98	0.99	350.49
NaOAc	35.2	44.6	51.66	1016.42	3.21	0.17	1.07	0.70	1.41	0.63	4.04	0.98	366.24
$MgOAc_2$	37.1	45.0	112.07	1045.88	3.23	0.19	1.79	1.06	1.28	0.63	3.88	0.93	364.07
EDTA-Na_2	35.7	44.5	88.23	989.22	3.20	0.11	1.28	0.85	0.58	0.47	3.96	0.89	296.90

Table S3 - Distillate parameters used to calculate permeate flux and polarizations in FO and MD processes

Solute	**T_D (°C)**	**C_D ($g.L^{-1}$)**	**ρ_D ($kg.m^{-3}$)**	**μ_D (mPa.s)**	**$k_{f.D}$ ($W.m^{-1}.K^{-1}$)**	**$c_{p.D}$ ($kJ.kg^{-1}.K^{-1}$)**	**$a_{w.D}$**	**h_D ($W.m^{-2}.K^{-1}$)**
NaCl	25.7	0.00	996.78	0.88	0.61	4.18	1.00	365.92
$MgCl_2$	26.2	0.00	996.66	0.87	0.61	4.18	1.00	366.23
NaOAc	24.9	4.00	996.98	0.89	0.61	4.18	0.99	365.36
$MgOAc_2$	23.6	9.53	997.27	0.92	0.61	4.18	0.96	364.53
EDTA-Na_2	24.4	26.21	997.09	0.90	0.61	4.18	0.93	365.04

Table S4- pH of feed solution, DS and distillate

Solute	$pH_{feed,final}$	$pH_{DS,inicial}$	$pH_{DS,final}$	$pH_{D,final}$
NaCl	7.0	6.5	4.7	5.8
$MgCl_2$	5.3	5.6	3.8	6.5
NaOAc	8.1	8.5	7.6	4.8
$MgOAc_2$	8.5	8.0	7.7	5.4
EDTA-Na_2	5.0	4.1	4.1	7.8

Table S5 - Criteria, weights and scores used in TOPSIS for selection of draw solute

Criteria	Criteria type	Weight	NaCl	$MgCl_2$	NaOAc	$MgOAc_2$	EDTA-Na_2
J_{FO} ($L.m^{-2}.h^{-1}$)	Benefit	3	4.78	3.64	4.57	4.82	2.81
J_{MD} ($L.m^{-2}.h^{-1}$)	Benefit	3	3.80	3.35	4.01	3.06	3.00
J_s ($g.m^{-2}.h^{-1}$)	Cost	3	3.00	0.72	2.57	4.58	3.28
J_{sMD} ($g.m^{-2}.h^{-1}$)	Cost	3	0.00	0.00	0.15	0.31	0.68
SEC_{pump} ($kW.m^{-3}.d^{-1}$)	Cost	3	0.155	0.190	0.155	0.175	0.221
DS cost ($US\$.L^{-1}$)	Cost	2	0.11	0.49	0.63	4.20	1.39
DS makeup cost ($U\$.m^{-3}$)	Cost	3	2.08	2.89	7.58	40.41	22.85
$R_{FO.EE2}$ (%)	Benefit	2.25	93.47	94.05	88.03	95.13	91.90
$R_{FO.BET}$ (%)	Benefit	1.5	83.34	91.12	99.04	62.87	71.98
$R_{FO.FEN}$ (%)	Benefit	1.8	99.67	89.44	86.33	95.65	99.47
$R_{FO.FLU}$ (%)	Benefit	2.25	74.75	76.49	69.59	80.45	89.49
$R_{FO.KET}$ (%)	Benefit	1.65	70.71	67.91	80.89	79.74	92.32
$R_{FO.LOR}$ (%)	Benefit	1.65	87.10	94.09	88.39	88.51	61.06
$R_{g.PRE}$ (%)	Benefit	1.65	76.74	83.18	76.91	61.24	87.39
$R_{g.EE2}$ (%)	Benefit	4.5	95.87	96.34	96.53	95.79	95.85
$R_{g.BET}$ (%)	Benefit	3	99.37	99.32	99.35	99.24	99.18
$R_{g.FEN}$ (%)	Benefit	3.6	99.79	99.78	99.79	99.75	99.73
$R_{g.FLU}$ (%)	Benefit	4.5	99.90	99.89	99.90	99.88	99.87
$R_{g.KET}$ (%)	Benefit	3.3	93.61	93.10	87.22	84.67	97.70
$R_{g.LOR}$ (%)	Benefit	3.3	99.87	99.86	99.86	99.84	99.82
$R_{g.PRE}$ (%)	Benefit	3.3	99.83	99.85	98.14	99.83	99.83

Methodology TOPSIS (*Technique for Order Preference by Similarity to Ideal Solution*) [1,2]

Step 1: Construction of the decision matrix (C) with m alternatives and n criteria.

$$C = \begin{bmatrix} c_{11} & \cdots & c_{1n} \\ \vdots & \ddots & \vdots \\ c_{m1} & \cdots & c_{mn} \end{bmatrix}$$

Where c_{ij} is the observed values of parameters for each alternative.

Step 2: Normalization of the initial matrix C by vector normalization method, to form the standardized decision matrix $R = (r_{ij})_{mxn}$.

$$r_{ij} = \frac{x_{ij}}{\sum_{i=1}^{m} x_{ij}^2}, \text{ i = 1, 2, ..., m; j = 1, 2, ..., n.}$$

$$R = \begin{bmatrix} r_{11} & \cdots & r_{1n} \\ \vdots & \ddots & \vdots \\ r_{m1} & \cdots & r_{mn} \end{bmatrix}$$

Step 3: Calculation of the weighted normalized matrix (A):

$$a_{ij} = w_{ij}\, x\, r_{ij}$$

Where a_{ij} is the weighted standardized value w_{ij} is the weight of each parameter.

Step 4: Determination of the positive and negative ideal reference points. A^+ represents the positive ideal solution and A^- is the negative ideal solution.

$$A^+ = (a_1{}^+, a_2{}^+, \dots, a_m{}^+)$$

$$A^- = (a^-, a_2{}^-, \dots, a_m{}^-)$$

and

$$a_j{}^+ = \left(max_i a_{ij}, j \in j_1; min_i a_{ij}, j \in j_2\right)$$

$$a_j{}^- = (min_i a_{ij}, j \in j_1; max_i a_{ij}, j \in j_2)$$

Where j_1 and j_2 represents the benefit criteria and the cost criteria. Therefore, for benefit criteria, the reference point for the positive ideal solution is the maximum value obtained for the alternatives and the reference point for the negative ideal solution is the minimum value for this criteria.

Step 5: Calculation of the Euclidean distances between the alternative (A_i) and the positive ideal solution (A^+) and A_i and the negative ideal solution (A^-)

$$D_i^+ = \sqrt{\sum_{j=1}^{n} \left(a_j{}^+ - a_{ij}\right)^2} \; with \; i = 1, \ldots, m.$$

$$D_i^- = \sqrt{\sum_{j=1}^{n} \left(a_j{}^- - a_{ij}\right)^2} \; with \; i = 1, \ldots, m.$$

Step 6: Calculation of similarities to the positive ideal solution

$$\mathrm{R}_i^+ = \frac{D_i{}^-}{D_i{}^+ + D_i{}^-}$$

Step 7: Rank the alternatives according to the similarities to the positive ideal solution values in descending order.

[1] P.P. Kalbar, S. Karmakar, S.R. Asolekar, Selection of an appropriate wastewater treatment technology: A scenario-based multiple-attribute decision-making approach, Journal of Environmental Management. 113 (2012) 158–169. https://doi.org/10.1016/j.jenvman.2012.08.025.

[2] P. Li, H. Qian, J. Wu, J. Chen, Sensitivity analysis of TOPSIS method in water quality assessment: I. Sensitivity to the parameter weights, Environ Monit Assess. 185 (2013) 2453–2461. https://doi.org/10.1007/s10661-012-2723-9.

Appendix C – Supplementary material chapter 3

1 Composition of the synthetic wastewater

Table S1 – Composition of the synthetic wastewater used as feed solution in the AnOMBR-MD

Component	**Concentration (mg L^{-1})**
Meat extract	208
Starch	114
Sucrose	35
$NaHCO_3$	200
KH_2PO_4	120
NaCl	250
$CaCl_2.6H_2O$	2.68
$MgCl_2.2H_2O$	1.53
LAS (tensoative)	15
Soybean oil	51

Table S2 – Physicochemical characterization of the synthetic wastewater used as feed solution in the AnOMBR-MD

Parameter	**Value**
pH	8.4 ± 0.2
Electrical conductivity (µS cm^{-1})	1182 ± 68.7
COD (mg L^{-1})	441 ± 57.3
DOC (mg L^{-1})	122.6 ± 4.5
Mg^{2+} (mg L^{-1})	4.7 ± 2
Cl^- (mg L^{-1})	194 ± 10.8
P-PO_4^{3-} (mg L^{-1})	29.9 ± 1.5
N-NH_4^+ (mg L^{-1})	6.4 ± 1.9
Alkalinity (mg$CaCO_3$ L^{-1})	184.5 ± 14.7
VFA (mgHAc L^{-1})	33.6 ± 7.3

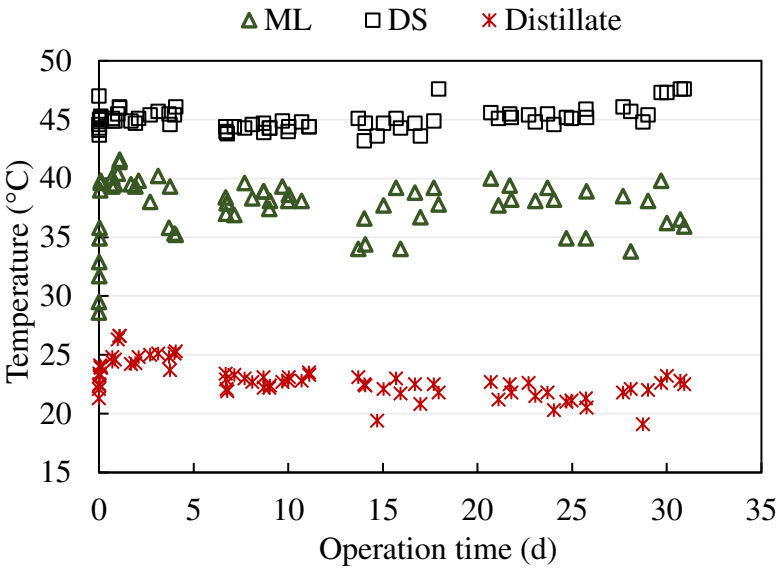


Figure S1 - Temperature during AnOMBR-MD operation.

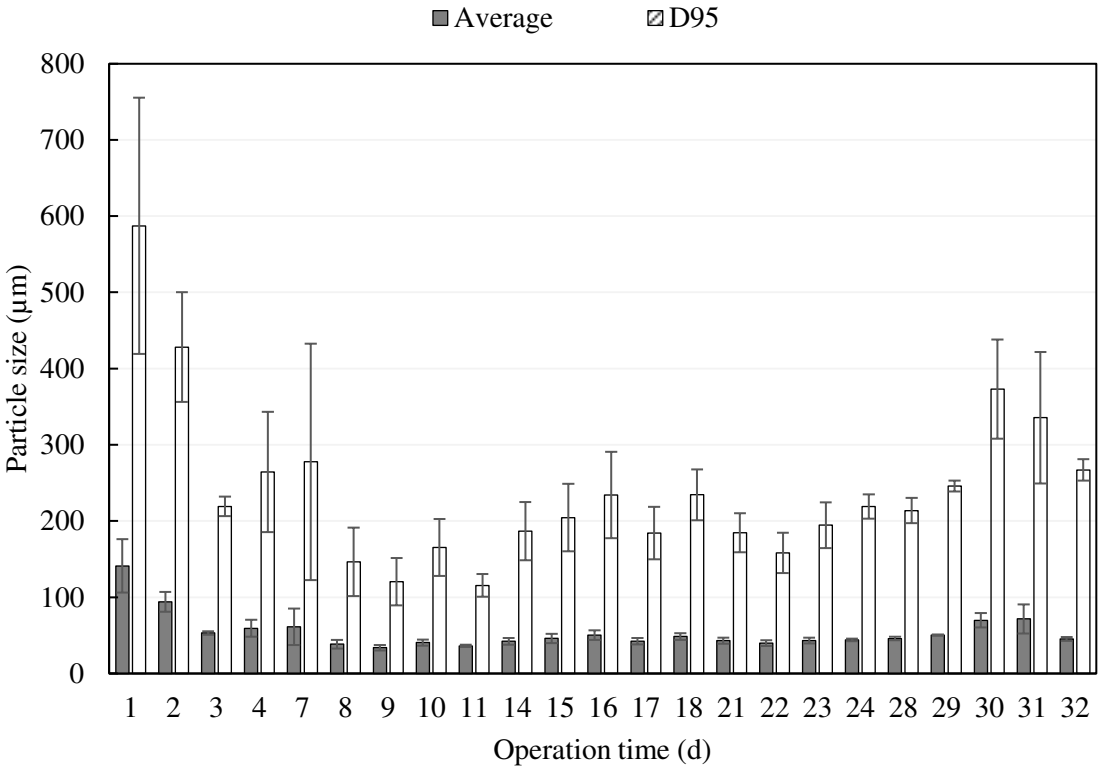


Figure S2 – Particle size distribution during AnOMBR-MD operation.

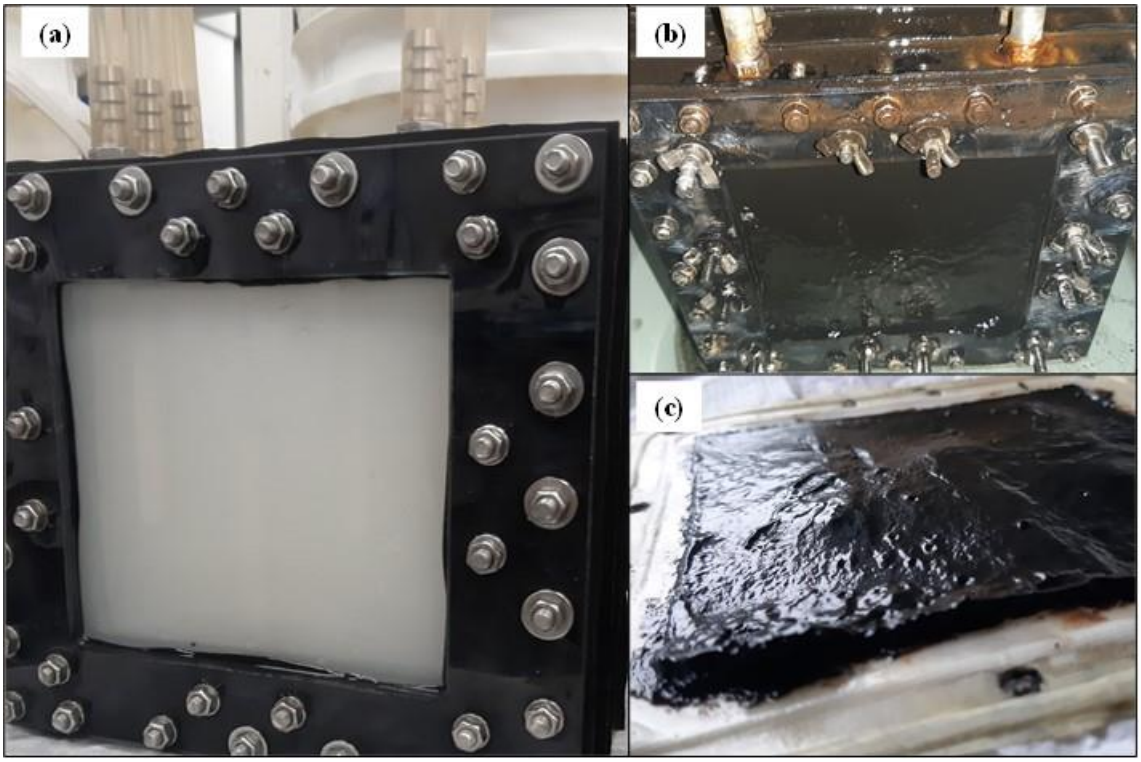


Figure S3 - (a) FO-MD hybrid module with a pristine FO membrane and (b) after 42 days of operation; and (c) fouled FO membrane.

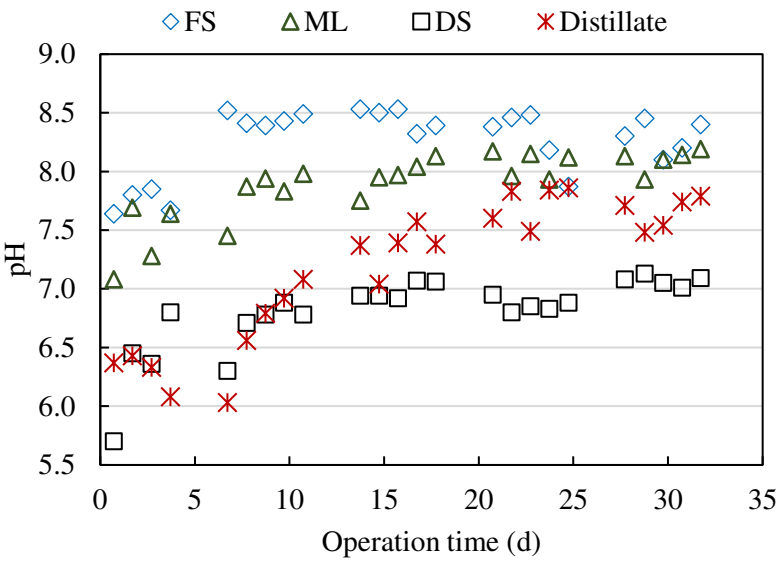


Figure S4 - pH during AnOMBR-MD operation.

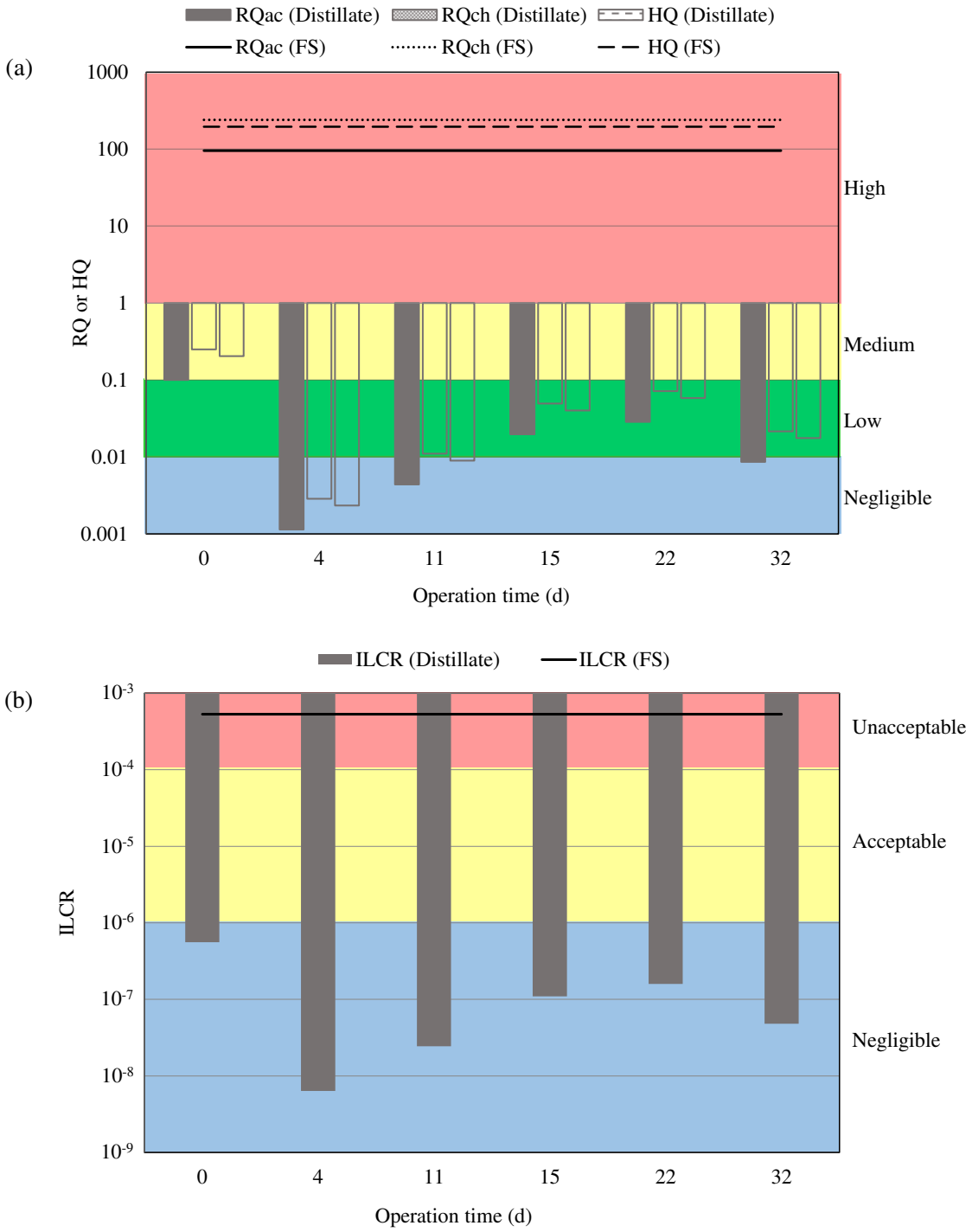


Figure S5 - (a) Environmental and human health risks, and (b) incremental lifetime cancer risk for AnOMBR-MD feed solution (FS) and distillate, considering the estrogenic activity.