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OSMOTIC BIOREACTOR COMBINED WITH REVERSE OSMOSIS AND UV/H_2O_2 TO TREAT WASTEWATER CONTAINING PHARMACEUTICALS AND PRODUCE HIGH QUALITY REUSE WATER

Jessica Rodrigues Pires da Silva

Tese de Doutorado apresentada ao Programa de Pós-Graduação em Engenharia Química, COPPE, da Universidade Federal do Rio de Janeiro, como parte dos requisitos necessários à obtenção do título de Doutor em Engenharia Química.

Orientadores: Cristiano Piacsek Borges
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BIOREATOR OSMÓTICO COMBINADO COM OSMOSE INVERSA E UV/H_2O_2 PARA TRATAMENTO DE EFLUENTE CONTENDO FÁRMACOS E PRODUÇÃO DE ÁGUA DE REÚSO DE ALTA QUALIDADE

Jessica Rodrigues Pires da Silva
Março/2021

Orientadores: Cristiano Piacsek Borges
Fabiana Valéria da Fonseca

Programa: Engenharia Química

O objetivo desta Tese foi avaliar os processos de biorreator osmótico com membranas (OBRM), osmose inversa (OI) e oxidação avançada com ultravioleta e peróxido de hidrogênio (UV/H_2O_2) para o tratamento de efluente sintético visando a remoção de fármacos e produção de água de reúso. A combinação do OBRM com a OI é imprescindível quando se pretende reusar a água, já que o OBRM sozinho gera somente solução extratora (SE) diluída. Nesse trabalho, o sal pirofosfato de potássio ($K_4P_2O_7$) foi usado como SE, e a OI foi usada para reconcentrar a SE. O permeado da OI é a água de reúso. Os resultados mostraram que com $K_4P_2O_7$ se obteve baixa permeabilidade inversa de sais (0.05 LMH) enquanto se manteve atividade biológica no biorreator, medida em termos de taxa de consumo de oxigênio. A água de reúso produzida teve concentrações de nitrito, nitrato e dos fármacos sulfametoxazol, carbamazepina e diclofenaco 4, 10, 74, 6 e 4 vezes menores, respectivamente, do que as encontradas no permeado de OI após um BRM convencional, e não houve declínio de fluxo de permeado na OI após o OBRM. Constatou-se experimentalmente a permeação de fármacos do biorreator para a SE em quantidades relevantes, alcançando concentrações na faixa de $\mu g.L^{-1}$ após 72h de operação contínua. Dose de UV de 816 $mJ.cm^{-2}$ com H_2O_2 de 30 $mg.L^{-1}$ removeu mais de 91% de todos esses fármacos acumulados na SE. Esses resultados demonstram a viabilidade técnica do processo combinado. Em termos de viabilidade econômica, o custo mínimo da água de reúso ficou em USD 1,23 por m^3 de água produzida.

Abstract of Thesis presented to COPPE/UFRJ as a partial fulfillment of the requirements for the degree of Doctor of Science (D.Sc.)

OSMOTIC BIOREACTOR COMBINED WITH REVERSE OSMOSIS AND UV/H_2O_2 TO TREAT WASTEWATER CONTAINING PHARMACEUTICALS AND PRODUCE HIGH QUALITY REUSE WATER

Jessica Rodrigues Pires da Silva
March/2021

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Department: Chemical Engineering

The objective of this Thesis was to evaluate the processes of osmotic membrane bioreactor (OMBR), reverse osmosis (RO) and advanced oxidation with ultraviolet and hydrogen peroxide (UV/H_2O_2) for the treatment of synthetic wastewater, aiming removal of pharmaceuticals and production of reuse water. The combination of OMBR and RO is essential when the goal is to reuse water, since OMBR alone generates only diluted draw solution (DS). In this work, potassium pyrophosphate salt ($K_4P_2O_7$) was used as DS, and RO was employed to reconcentrate the DS. The RO permeate corresponded to the reuse water. The results showed that, by using $K_4P_2O_7$, low reverse salt permeability (0.05 LMH) was obtained while maintaining the biological activity in the bioreactor, measured in terms of oxygen uptake rate. Reuse water had concentrations of nitrite, nitrate and the pharmaceuticals sulfamethoxazole, carbamazepine and diclofenac 4, 10, 74, 6 and 4 times lower, respectively, than those found in RO permeate after a conventional MBR, and there was no water flux decline in the RO employed after OMBR. It was demonstrated experimentally that permeation of pharmaceuticals from the bioreactor to the DS occurs at considerable levels, reaching concentrations in the range of $\mu g.L^{-1}$ after 72h of continuous operation. A UV dose of 816 $mJ.cm^{-2}$ with H_2O_2 of 30 $mg.L^{-1}$ removed more than 91% of all pharmaceuticals accumulated in the DS. These results demonstrate the technical feasibility of the combined process. In terms of economic feasibility, the minimum cost of reused water was USD 1.23 per m³ of water produced.

SUMMARY

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List of Abbreviations

ACT - Acetaminophen

AL-DS – Active layer on the draw solution

AL-FS – Active layer on the feed side

AOPs – Advanced Oxidation Processes

API – Active Pharmaceutical Ingredient

AS – Activated Sludge

BOD_5 – 5-day Biological Oxygen Demand

CAPEX – Capital Expenditures

CBZ – Carbamazepine

COD – Chemical Oxygen Demand

CTA – Cellulose TriAcetate

DI – DeIonized

DIF – Diclofenac

DO – Dissolved Oxygen

DOC – Dissolved Organic Carbon

DPR – Direct Potable Reuse

DS – Draw Solution

ECP – External Concentration Polarization

EE2 – 17-α-ethinylestradiol

EPA – Environmental Protection Agency

FO – Forward Osmosis

FS – Feed Solution

GC – Gas Chromatography

HPLC - High-Performance Liquid Chromatography

HRT – Hydraulic Retention Time

ICP –Internal Concentration Polarization

IPR – Indirect Potable Reuse

LC – Liquid Chromatography

MBR – Membrane Bioreactor

MF – Microfiltration

ML – Mixed Liquor

MLVSS – Mixed Liquor Suspended Volatile Solids

MPs – Micropollutants

MQL – Method Quantification Limit

MS – Mass spectrometry

MW – Molecular Weight

NF – Nanofiltration

NOM – Natural Organic Matter

NPV – Net Present Value

OMBR - Osmotic Membrane Bioreactor

OPEX – Operating Expenses

OUR – Oxygen Uptake Rate

PAH - Polycyclic Aromatic Hydrocarbon

PhACs – Pharmaceutically Active Compounds

RO – Reverse Osmosis

RSF – Reverse Salt Flux

SMP – Soluble Microbial Products

SMX – Sulfamethoxazole

SPE – Solid-phase extraction

SRT – Solid Retention Time

SOUR – Specific Oxygen Uptake Rate

TC - Total Cost

TFC – Thin-Film Composite

TOC – Total Organic Carbon

UF – Ultrafiltration

UM – United Nations

UN – United Nations

US – United States

UV – Ultraviolet

WHO – World Health Organization

WWTP – Wastewater Treatment Plants

List of Symbols

H_2O_2 – Hydrogen Peroxide

•OH – Hydroxyl radicals

$K_4P_2O_7$ – Potassium Pyrophosphate

NaCl – Sodium Chloride

Js – Reverse salt flux

Jw – Water flux

A – Pure water permeability

Π – Osmotic pressure

B – Solute permeability

LMH – Liter per m^2 per hour

Δt – Time interval

Vt – volume of solution at time t

Ct – concentration of a solute in solution at time t

ΔC – Solute concentration difference between two sides of a membrane

k - Time-based pseudo first-order rate constant for photolysis of compounds

S – structural parameter of a membrane

Chapter 1 – Thesis Introduction

1.1 Introduction

Freshwater is essential for every activity in the society, but notwithstanding its apparent abundance on Earth, it is actually a limited resource. Too much of it is wasted or unsustainably managed, and the increasing environmental pollution, industrial and agricultural demand further augment strain on water resources, already unevenly distributed on Earth (CAPODAGLIO, 2020, LUJÁN-FACUNDO, SOLER-CABEZAS, *et al.*, 2017). Freshwater scarcity already affects to some extent 2 billion of people around the world (KAPLAN, MAMANE, *et al.*, 2020) and is expected to worsen due to population growth and increase of water use per capita (DELLI COMPAGNI, GABRIELLI, *et al.*, 2020), which leads to an estimative that, within the next 50 years, over forty percent of the world's population will live in countries facing water stress or scarcity at least one month per year ((BICHAI, KAJENTHIRA GRINDLE, *et al.*, 2018). Meanwhile there is the emerging concern of how climate changes will affect the water resources worldwide because of projected changes in precipitation patterns, temperature, and other climate variables, raising questions whether the future hydrological cycles will follow the historical record and be able to maintain water resources as they are now in quality and availability (UNITED NATIONS WATER, 2017).

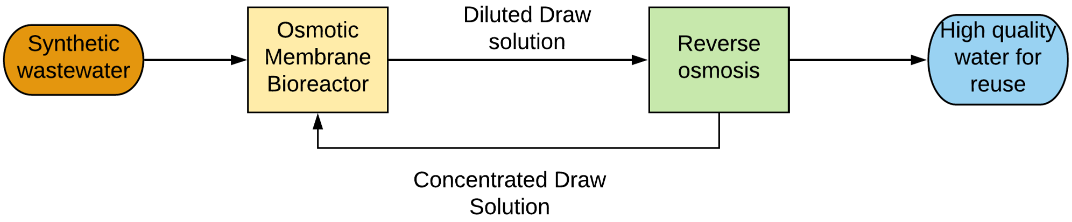
As a result of this worrisome scenario, widespread fresh water scarcity has become a concern. Thus, there is a growing demand for alternatives to increase and guarantee the fresh water supply not only for human consumption but also for industry and agricultural uses (BICHAI, KAJENTHIRA GRINDLE, *et al.*, 2018, CAPODAGLIO, 2020, SOLLER, EFTIM, *et al.*, 2019). The two climate-independent water sources are water desalination and water reuse (FURLONG, JEGATHEESAN, *et al.*, 2019), but the reuse of wastewater originating from urban Wastewater Treatment Plants (WWTPs), known as water reuse or water reclamation, is identified as the main sustainable measure to alleviate fresh water scarcity, not only because it typically costs less, but also because has a smaller carbon and energy footprint (DELLI COMPAGNI, GABRIELLI, *et al.*, 2020, FURLONG, JEGATHEESAN, *et al.*, 2019). The reuse of wastewater for both potable and non-potable applications has been presented internationally as a pragmatic measure to address water scarcity and environmental pollution for a sustainable development (UNITED NATIONS WATER, 2017).

When considered individually, each unit process for wastewater treatment has its merits and shortcomings in regards to attaining water reuse, as no single treatment can provide an absolute barrier to all types of contaminants, especially when considering emerging contaminants (CAPODAGLIO, 2020, PIRAS, SANTORO, *et al.*, 2020). This issue is particularly relevant for the removal of Pharmaceutically Active Compounds (PhACs) from water. PhACs are a class of emerging micropollutants that contain active ingredients designed to have effects on living organisms even in very low concentrations and are present in raw municipal wastewaters and some industrial wastewaters (TIJANI, FATOBA, *et al.*, 2016, TIWARI, SELLAMUTHU, *et al.*, 2017). This class is worrisome as it is established that many PhACs are recalcitrant to conventional biological treatment which, therefore, cannot be considered an absolute barrier to their complete removal from wastewater (FALÅS, WICK, *et al.*, 2016, IKEHATA, EL-DIN, *et al.*, 2008, NSENGA KUMWIMBA, MENG, 2019). Considering the ecotoxic potential of several PhACs even at trace concentrations (LINDIM, DE ZWART, *et al.*, 2019, SANTOS, ARAÚJO, *et al.*, 2010, VASQUEZ, LAMBRIANIDES, *et al.*, 2014), a high removal of PhACs becomes of paramount importance for water reuse applications.

To overcome process-specific limitations, particularly in regard to attaining high removal of PhACs from wastewater, a multi-barrier approach is adopted, where two or more treatment “barriers” are combined in order to increase the number of safeguards for pollutants removal, thus increasing process safety and water quality (CAPODAGLIO, 2020). A widely employed multi barrier treatment is secondary treatment followed by low-pressure membrane filtration (microfiltration- MF or ultrafiltration-UF) and reverse osmosis (RO) (BUSETTI, RUFF, *et al.*, 2015, CAPODAGLIO, 2020, GARCIA, MORENO, *et al.*, 2013, HOLLOWAY, MILLER-ROBBIE, *et al.*, 2016, PIRAS, SANTORO, *et al.*, 2020, VALLADARES LINARES, LI, *et al.*, 2016). More recently, there is a tendency for direct integration of biological treatment with MF as a membrane bioreactor (MBR) (CARTAGENA, EL KADDOURI, *et al.*, 2013, GÜNDOĞDU, JARMA, *et al.*, 2019, XIAO, LIANG, *et al.*, 2019).

MBR-RO has been explored in literature for water reuse applications including for PhACs removal (BESHA, GEBREYOHANNES, *et al.*, 2017, XIAO, LIANG, *et al.*, 2019). Its main disadvantages can be attributed to the high fouling observed in the RO membranes, to the generation of RO retentate that requires further treatment for disposal; and to the presence of some PhAC residues, in concentrations of ng.L^{-1}, even in the RO permeate (BUSETTI, RUFF, *et al.*, 2015, CARTAGENA, EL KADDOURI, *et al.*, 2013, CHON, KYONGSHON, *et al.*, 2012, LUO, Wenhai, PHAN, *et al.*, 2017, SAHAR, DAVID, *et al.*, 2011). Considering these disadvantages and the need to develop improved systems, this Thesis was developed with the aim to evaluate experimentally an osmotic membrane bioreactor (OMBR), which is a modification of an MBR, combined with reverse osmosis for wastewater treament with high PhAC removal. In an OMBR, microfiltration membranes are replaced by Forward Osmosis (FO) membranes. Figure 1 presents a scheme of the arrangement proposed in this Thesis.

Figure 1: Scheme of the proposed process: OMBR-RO



An aerobic OMBR couples activated sludge processes with a non-porous, semi-permeable FO membrane (HOLLOWAY, ACHILLI, *et al.*, 2015). It is an unconventional membrane process in the sense that the driving force to permeate water through the FO membrane is not applied pressure as in MF, but rather the osmotic pressure difference across the membrane created by the use of a Draw Solution (DS) of high osmotic pressure on the other side of the membrane (ZHANG, Mengyu, ZUO, *et al.*, 2018), in this case, a solution of inorganic salt potassium pyrophosphate ($K_4P_2O_7$). Water from the mixed liquor in the bioreactor permeates to the side of the DS, diluting it. In this case, the posterior RO stage serves not only as a posterior treatment stage to produce fresh/reuse water, but also for the concentration of the DS diluted at the OMBR stage (LUJÁN-FACUNDO, SOLER-CABEZAS, *et al.*, 2017). After DS is reconcentrated, it is recycled to the bioreactor.

Advantages and drawbacks of the OMBR-RO technology were explored in the present Thesis through experiments using a laboratory-scale prototype of OMBR and a

RO system. Reclaimed water (i.e. RO permeate) was evaluated in terms of quality, considering removal not only of organic matter and nutrients but also of five PhACs of interest (diclofenac, carbamazepine, acetaminophen, sulfamethoxaole and ethinylestradiol) in environmentally relevant concentrations. Quality of the reuse water was compared to that obtained by the more conventional MBR-RO treatment, in order to verify whether replacing an MBR for an OMBR is justified from the point of view of gains in water quality. It is noted that, considering the experimental results, there was a need to include an oxidation step to remove PhACs that accumulated in the DS during the OMBR continuous operation, due to diffusion of these solutes from the mixed liquor to the DS. Thus, experiments were included to verify the feasibility of using UV/H_2O_2 for this purpose. Preliminary process cost estimation (capital expenditures and operating expenses) was also done to contribute to the analysis of the feasibility of OMBR-RO with UV/H_2O_2 compared to a more conventional scenario of MBR-RO with UV/H_2O_2 for treatment of RO retentate.

1.2 Hypotheses and Objectives

Based on the review of the existing literature, the following hypotheses have been raised:

- The selected PhACs cause adverse effects on activated sludge biomass, so this biomass needs to be acclimated before inoculated to the OMBR.

- None of the selected PhACs are completely removed, i.e below method detection limit, by the activated sludge treatment even at optimized operating conditions e.g. high hydraulic and solid retention times.

- The combination of OMBR with RO obtains high quality reuse water, considering removal of organic matter, nutrients and PhACs, and this quality is superior to that obtained by the more conventional MBR-RO process.

- In OMBR there will be less reverse salt flux due to the use of potassium pyrophosphate as draw solute. Consequently, little or no impact will be observed on the acclimated biomass activity. In addition, the water flux decline will be small in both the FO membrane and the subsequent RO, because of low fouling propensity and high retention of low molecular size compounds by the FO membrane.

- There is diffusion of PhACs to the draw solution during the continuous operation of OMBR and UV/H_2O_2 is a possible alternative for the elimination of these compounds from the DS.

The main objective of this Thesis is a comprehensive evaluation of an innovative process composed of osmotic membrane bioreactor, reverse osmosis and UV/H_2O_2 to treat synthetic wastewater, remove PhACS and produce high quality water for reuse. Specific objectives are:

1. To study the effects of PhACs on the activated sludge biomass, evaluating the need to acclimate the sludge biomass prior to inoculation in the osmotic bioreactor.

2. To study the removal of each PhAC by the activated sludge process, by the complementary UV/H_2O_2 and by the OMBR-RO.

3. To evaluate OMBR combined with RO in terms of i) biomass activity; ii) reverse salt flux; and iii) permeate flux obtained in OMBR and in the subsequent RO.

4. To evaluate the extension of PhACs accumulation in DS and, in the case this accumulation is high enough to be relevant, to assess whether UV/H_2O_2 can be used to eliminate these compounds from the DS.

5. To evaluate the quality of the final reuse water produced by the combined process (permeate of RO in OMBR-RO) in terms of organic matter, nutrients and PhACs removal, discussing implications for high quality water reuse and comparing the result to that obtained in a more conventional MBR-RO process.

1.3 Motivation

The interest in the use of membrane separation and advanced oxidation processes combined with biological processes for wastewater treatment is growing, due to their great potential for improving efficiency in terms of removing nutrients and emerging pollutants such as PhACs. Such high removals are required in the context of the high quality reuse water, a product whose demand tends to grow given the reality of increasing water scarcity in Brazil and worldwide. However, the applicability of these technologies in a combined and innovative manner is still a challenge, especially when concerning FO.

From a Chemical Engineering perspective, the improvement of these processes can be achieved in different ways, for example, by researching new, enhanced materials, by process modelling and optimization or by assessing experimentally the combined processes. The third approach was the one chosen in the present Thesis. It aimed to identify results already achievable with the current state of the art technology and analyzing them from an engineering perspective. Research was directed to some of the knowledge gaps identified in literature, seeking to investigate them, therefore contributing to the advancement of these technologies.

In the analysis of the state of the art of OMBR-RO, several potential advantages of the use of these technologies are identified that directly address some of the drawbacks of MBR-RO, making them a promising alternative for investigation in a context where the ultimate goal is the obtention of high quality reuse water. Such potential advantages are presented in detail in the review of Chapter, but the main ones can be summarized as: i) the presence of the non-porous FO membrane in the reactor retains most soluble microbial products in the mixed liquor, reducing fouling and scaling potential on the RO membrane, thus reducing its cleaning requirements; ii) as RO retentate is also the regenerated draw solution, this stream is recirculated, not disposed, eliminating the need of disposing the RO retentate. Even if some treatment of this stream is necessary, it will be less expensive than the conventional process since few contaminants will be present in the current due to the high rejection of the FO membrane; iii) the presence of a double layer of non-porous membrane membranes, in contrast to only one in MBR-RO, could produce water of better quality, particularly considering the removal of PhACs

(BLANDIN, LE-CLECH, *et al.*, 2018, CORZO, DE LA TORRE, *et al.*, 2017, LUO, Wenhai, PHAN, *et al.*, 2017, SHAFFER, WERBER, *et al.*, 2015).

Thus, the present study was motivated to expand the know-how of membrane-based and advanced oxidation technologies combined with biological processes, by addressing these and other related topics that are on the frontier of knowledge for these technologies. It is hoped that it can leave a contribution to the advancement of the practice of high quality water reuse in Brazil and in the world. Specific innovations of the Thesis are:

- The salt used in the draw solution was potassium pyrophosphate because of its favorable properties for use in osmotic applications, such as low diffusivity and high rejection by size exclusion by FO membrane (due to the large hydrated radius of pyrophosphate), absence of toxicity, high osmotic pressure and high solubility in water. Despite these promising properties, this salt has not been tested so far in the literature for applications in OMBR.

- The possibility of PhACS diffusion to the draw solution in considerable amounts leading to accumulation has already been mentioned by some modelling works, however, seldom demonstrated experimentally, and never for the pharmaceuticals selected in this Thesis. Feasibility of employing an AOP to treat this specific saline current has not been explored, either.

- Effects of PhACs on the activity of activated sludge biomass, leading to observable effects on the quality of the biologically treated effluent, are well established in concentrations of mg.L^{-1}, but not in the concentration of µg.L^{-1}, which is the environmentally relevant concentration. In particular, this issue has not yet been explored for the PhACs selected in this Thesis.

1.4 Thesis Structure

This Thesis is divided in five chapters. In this Chapter 1, an introduction to the Thesis was given. Chapters 2, 3 and 4 are the chapters where results of the thesis are presented. Each chapter was based on a scientific article, although the chapters do not correspond exactly to the full article because they also contain supplementary information to support the discussion of the results. Chapter 5 presents the final considerations.

Chapter 2 was based on the article “Study of effects of pharmaceuticals on the activated sludge process combining advanced oxidation using ultraviolet/hydrogen peroxide to increase their removal and mineralization of wastewater”. In this chapter, preliminary results of the Thesis were presented. The results were mainly focused on the acclimation of the sludge from the bioreactor to the PhACs before their inoculation in the OMBR. This previous acclimation was necessary so that these compounds did not negatively influence the biological stage of the OMBR-RO process, due to their ecotoxic potential to microorganisms. Results regarding PhACs removal by activated sludge process and by UV/H_2O_2 are also presented. Finally, Chapter 2 presents the chromatographic method developed in partnership with the Oswaldo Cruz Foundation for the detection of PhACs in the water samples.

Chapter 3 was based on the article “Applicability of osmotic bioreactor using potassium pyrophosphate as draw solution combined with reverse osmosis for removal of pharmaceuticals and production of high quality reuse water”. In Chapter 3, results of the continuous operation of the OMBR prototype using potassium pyrophosphate as draw solution are presented, as well as results from the operation of the combined OMBR-RO process. This chapter also includes results of the quantification of PhACs in draw solution during long-term operation and results of the quality of reuse water produced by the OMBR-RO, discussing its implications for reuse.

Chapter 4 was based on the article “Technical-economical analysis of osmotic versus conventional membrane bioreactors integrated with reverse osmosis and UV/hydrogen peroxide for water reuse”. In this chapter, results regarding technical feasibility of employing UV/H_2O_2 to remove PhACs from draw solution to control the accumulation of PhACs during long-term operation were presented, considering this accumulation was experimentally proven in Chapter 3. This chapter also contains results of economic analysis, informing the minimum cost of treated water necessary for OMBR-RO-UV/H_2O_2 to be economically feasible. Experimental results obtained in Chapters 2 and 3 were used as input parameters for economic calculations in this chapter, and a comparison was made to a baseline scenario using a more conventional approach (MBR-RO with AOP in retentate).

Chapter 5 presented the final considerations of the Thesis and suggestions for future work. The references of all chapters are presented together in the References section after Chapter 5.

1.5 Publications of the Thesis

Article “Study of effects of pharmaceuticals on the activated sludge process combining advanced oxidation using ultraviolet/hydrogen peroxide to increase their removal and mineralization of wastewater” was published as a original research article in the Journal of Environmental Chemical Engineering, Volume 9, Issue 1, February 2021, available at https://doi.org/10.1016/j.jece.2020.104576. Moreover, the article “A Critical Review of Criteria Used For the Selection of Pharmaceuticals and Personal Care Products in Different Environmental Matrices” was published in Environmental Pollution and Protection, Vol. 5, No. 1, March 2020, https://dx.doi.org/10.22606/epp.2020.51002 . A short version of this article has been incorporated as a literature review in chapter 2.

Article “Applicability of osmotic bioreactor using potassium pyrophosphate as draw solution combined with reverse osmosis for removal of pharmaceuticals and production of high quality water reuse” was submitted to a scientific journal.

Article "Technical-economical analysis of osmotic versus conventional membrane bioreactors integrated with reverse osmosis and UV/hydrogen peroxide for water reuse" is being finalized, with the intention of submitting it a scientific journal.

Partial results of this Thesis were presented in poster format at the 22nd Brazilian Congress of Chemical Engineering (COBEQ), held in São Paulo in 2018.

Two other articles were produced throughout the development of the thesis as co-author: “Ethinylestradiol removal of membrane bioreactor efluent by reverse osmosis and UV/H_2O_2: A technical and economic assessment”, published in the Journal of Environmental Management 282 (2021) 111948, https://doi.org/10.1016/j.jenvman.2021.111948 and “Effects of influent composition on biological activity, acclimation time and microbial community profile of activated sludge” published in the International Journal of Development Research Vol. 11, Issue, 01, January, 2021, https://doi.org/10.37118/ijdr.20958.01.2021.

Chapter 2 - Study of effects of pharmaceuticals on the activated sludge process combining advanced oxidation using ultraviolet/hydrogen peroxide to increase their removal and mineralization of wastewater

2.1 Introduction and objectives

Pharmaceutically Active Compounds (PhACs) are a class of micropollutants that are particularly worrisome from an environmental point of view, since at very low concentrations (ng.L^{-1}-µg.L^{-1}) they can present adverse effects on aquatic wildlife . As a consequence of the increasing worldwide consumption of pharmaceuticals – a direct result of a combination of factors including population growth, fast development of medical science, ageing of the population and healthcare professionals' prescription habits - PhACs are now frequently detected in raw domestic and industrial wastewaters ((GHAFOORI, MOWLA, *et al.*, 2015, LE CORRE, ORT, *et al.*, 2012, LINDBERG, ÖSTMAN, *et al.*, 2014, MOWLA, MEHRVAR, *et al.*, 2014, TIJANI, FATOBA, *et al.*, 2016).

Biological processes, and activated sludge (AS) in particular, are very common and used routinely around the world in WasteWater Treatment Plants (WWTP) for the treatment of these wastewaters (METCALF, EDDY, 2003, MOWLA, MEHRVAR, *et al.*, 2014, THIEBAULT, BOUSSAFIR, *et al.*, 2017). However, several studies have been showing that the increase in PhACs concentrations on raw wastewater might create side effects to the activated sludge biomass by changing microbial community profiles and gene expressions (HARB, WEI, *et al.*, 2016b, KRAIGHER, KOSJEK, *et al.*, 2008, KRUGLOVA, GONZALEZ-MARTINEZ, *et al.*, 2017, ZHAO, Renxin, FENG, *et al.*, 2019). Furthermore, it has been demonstrated that some PhACS in synthetic wastewaters affect, to some extent, biochemical activity and organic matter and nutrient removal (AMORIM, MOREIRA, *et al.*, 2016, LIWARSKA-BIZUKOJC, GALAMON, *et al.*, 2018, OH, CHOI, 2020, ZHANG, Yingying, GENG, *et al.*, 2016, ZHOU, LI, *et al.*, 2019). Nonetheless, such studies are still limited to only one or two PhAC at a time (ZHANG, Yingying, GENG, *et al.*, 2016, ZHOU, LI, *et al.*, 2019) and/or unreallistic concentrations, e.g., in a range of mg.L^{-1} (OH, CHOI, 2020, ZHOU, LI, *et al.*, 2019), missing the synergistic effects that might happen during wastewater treatment in environmental relevant concentrations. As a result, a clear understanding of PhAcs effects on activated sludge biomass is still missing, especially when considering a mixture of PhAcs in µg.L^{-1}-ng.L^{-1} concentrations.

Assuming that such effects do occur, even if temporarily, which is a hypothesis of the present Thesis, it is necessary to acclimatize the activated sludge. Acclimatization results in the adaptation of the system to its operational conditions, where sludge microbes develop natural resistance to variations in such conditions (POURSAT, VAN SPANNING, *et al.*, 2020), thereby avoiding inhibition of biological activity that could be attributed to other factors in the process when in fact they were the result only of the temporary stress involved in the presence of exogenous compounds introduced, in the case, PhACs. Considering an Osmotic bioreactor (OMBR) is inoculated using activated sludge, there can be no effect on activated sludge biomass activity created by the addition of PhACs (nor by the use of synthetic feed wastewater), so as not to mask the possible effects that may arise from the typical operation of the osmotic bioreactor, effects that will be study in Chapter 3. Therefore, acclimatization of sludge to PhACs before inoculation to the OMBR is of paramount importance and was an objective of this Chapter.

Furthermore it is known that many PhACs are recalcitrante to conventional AS to some extent which depend on the PhAC (FALÅS, WICK, *et al.*, 2016, LUO, Yunlong, GUO, *et al.*, 2014, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009, THIEBAULT, BOUSSAFIR, *et al.*, 2017), so in this Chapter, removal of selected PhACs by the activated sludge during and after acclimatization was investigated, as well as PhACs removal by the advanced treatment of UV/H_2O_2. It is noteworthy that the use of UV/H_2O_2 combined with biological treatment, employing relatively small doses of H_2O_2 and UV (3-25 $mg.L^{-1}$ and less than 2700 $mJ.cm^{-2}$, respectively), reportedly achieves high levels (91-100%) of removal for many PhACs, including the five selected in this Thesis – 17-α-ethinylestradiol (EE2), sulfamethoxazole (SMX), diclofenac (DIF), carbamazepine (CBZ) and acetaminophen (ACT) (GIANNAKIS, GAMARRA VIVES, *et al.*, 2015, JAMES, GERMAIN, *et al.*, 2014, LEE, Yunho, GERRITY, *et al.*, 2016, SARKAR, ALI, *et al.*, 2014, SILVA, Larissa L.S., SALES, *et al.*, 2017). Nonetheless, none of these works concurrently achieve mineralization higher than 30%. Few authors achieve satisfactory mineralization (GIANNAKIS, GAMARRA VIVES, *et al.*, 2015, RODRÍGUEZ-CHUECA, LASKI, *et al.*, 2018, SARKAR, ALI, *et al.*, 2014). However, mineralization is highly desired, since under usual UV/H_2O_2 operating conditions, PhACs are degraded to transformation products (TPs) (BOURGIN, BOROWSKA, *et al.*, 2017, FATTA-KASSINOS, VASQUEZ, *et al.*, 2011) and there is a growing concern about TPs because of their unknown structures, which might make them equally or more toxic than their parent compounds (FATTA-KASSINOS, VASQUEZ, *et al.*, 2011, JUSTO, GONZÁLEZ, *et al.*, 2013). Therefore, in this chapter the conditions for mineralization of TPs and recalcitrant organics were assessed by means of removal of dissolved organic carbon in biologically treated effluent.

The objectives of this Chapter were:

- To acclimate activated sludge biomass firstly to synthetic municipal wastewater and, secondly, to the pharmaceuticals ACT, DIF, EE2, CBZ and SXM, so it can be used as inoculum to the osmotic bioreactor (corresponding to the specific objective 1);

- To assess the removal of ACT, DIF, EE2, CBZ and SMZ by the activated sludge process during and after completion of acclimatization, as well as by the complementary UV/H_2O_2 treatment (corresponding to the specific objective 2);

- To find the experimental condition (dose of UV and H_2O_2) that increases DOC removal concurrently with high PhACs removal from biologically treated effluent, so that it can be used as input parameter for economic considerations.

2.2 Literature Review

2.2.1 Micropollutants and pharmaceuticals

Definition

Micropollutants (MPs) are a broadly defined term that encompasses synthetic or naturally occurring compounds and their metabolites such as pharmaceuticals, including subclasses of antibiotics, painkillers, antiinflammatory, including those for veterinary medicine); personal care products; pesticides; herbicides; disinfection by-products; polycyclic aromatic hydrocarbons (PAHs); polychlorinated biphenyls (PCBs); endocrine disrupting compounds (such as steroid sex hormones, synthetic or natural) and industrial chemicals, including subclasses like solvents, corrosion inhibitors and fire retardants.

They have in common the fact that they occur in the various environmental matrices in very low concentrations – between the µg/L and ng/L. For these reason, they are also referred in literature as as trace organic compounds (LUO, Yunlong, GUO, *et al.*, 2014, TIJANI, FATOBA, *et al.*, 2016).

These complex compounds are polar or semi-polar and are known to exhibit both acidic and basic functional groups in aqueous medium. Besides, these substances are mobile and may bepersistent and bioaccumulate in wildlife (TIJANI, FATOBA, *et al.*, 2016). Their low concentration in the environment not only complicates the associated detection and analysis procedures but also create challenges for water and wastewater treatment processes (LUO, Yunlong, GUO, *et al.*, 2014). Their analysis require very sensitive analysis procedures, in general, liquid or gas chromatography methods, usually associated with high sensitivity detectors to improve the analytical response - mass spectrometry has been predominant in this sense. Micropollutants are considered emerging pollutants, in the sense they began to be reported routinely only in the last two decades as analytical techniques improved (TIJANI, FATOBA, *et al.*, 2016). Nowadays, they are found ubiquitously in the anthropogenically influenced water cycle including. surface, groundwater and even the sea around the world (BOLLMANN, SIMON, *et al.*, 2019, PITARCH, CERVERA, *et al.*, 2016).

Even if some of these compounds can originate from natural processes, for example some steroidal sex hormones released by females or PAHs, natural concentrations are low compared to the anthropogenically induced pollution. Besides, for most micropollutants, their natural background is negligible or even absent as they have no non-anthropogenic sources. Thus, the problem of water contamination caused by micropollutants is considered an issue arising from human activity. Recent studies even point out, for this reason, an increasing tendency to use some compounds to replace classic pollution indicators as inorganic ions to detect and quantify wastewater-derived pollution (WARNER, LICHA, *et al.*, 2019).

Micropollutants mainly originate from agricultural runoff, untreated wastewater and even wastewater discharge from wastewater treatment plants (WWTPs), which may comprise domestic, hospital, and industrial wastewaters. This is because many micropollutants show low removal rates during conventional wastewater treatment based on biological processes such as the activated sludge process or biofiltration, a fact well established in literature (BESHA, GEBREYOHANNES, *et al.*, 2017, FALÅS, WICK, *et al.*, 2016, GRANDCLÉMENT, SEYSSIECQ, *et al.*, 2017, LUO, Yunlong, GUO, *et al.*, 2014, WARNER, LICHA, *et al.*, 2019). This is because such plants have been designed targetting removal of organic matter, pathogenic microorganisms and in some cases, nutrientes, not micropollutants. Other entry points for MP recently started to be considered as important point sources, such as leachate landfill and industrial wastewaters, particularly those from the pharmaceutical, cosmetics, pesticides and sanitizing industries (LUO, Yunlong, GUO, *et al.*, 2014).

All of these contributions result in a broad spectrum of compounds entering the aquatic environment, where their perceived ecotoxicity has recently become a subject of intense debate due to their individual or synergistic actions and growing concern as more and more evidence of these ecotoxic effects becomes available even at the very low concentrations they occur at the environment (LINDIM, DE ZWART, *et al.*, 2019, LIU, LU, *et al.*, 2020, TIJANI, FATOBA, *et al.*, 2016, VASQUEZ, LAMBRIANIDES, *et al.*, 2014). Furthermore, a large number of locations and countries are known to practice *de facto* (unplanned) reuse, which occurs when wastewater is discharged to a source of drinking water (RICE, WESTERHOFF, 2015). In one way or another, if MP are not highly removed at the wastewater treatment stage, it will increase the probability of its occurrence in drinking water reservoirs.

Pharmaceutically Active Compounds (PhACs)[1], also known as Active Phamaceuticals Ingredients (API) are a class of micropollutants that can be found in drugs, including both therapeutic and veterinary, designed to cure and prevent the spread of diseases as well as adding value to human and animal life. They contain active ingredients that have been designed to have effects on living organisms, i.e.biologically active compounds, as they can pass through biological membranes and persist in the body for extended periods of time and are known to be persistent, bio-active and bio-accumulative (BOTTONI, CAROLI, *et al.*, 2010, PÉREZ-LEMUS, LÓPEZ-SERNA, *et al.*, 2019, TIJANI, FATOBA, *et al.*, 2016, TIWARI, SELLAMUTHU, *et al.*, 2017). From an environmental point of view, pharmaceuticals have distinctive characteristics

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[1] They can also be referred simply as “pharmaceuticals”.

compared to conventional chemical contaminants; the group comprises molecules of diverse structure, molecular weight and shape. They are made up of chemically complex molecules, usually polar and with more than one ionizable group; as a result, pH of the solution in which the molecules are found will affect both their properties and the degree of ionization (ALONSO, EL KORI, *et al.*, 2018). These same characteristics make these compounds particularly worrysome for aquatic wildlife and, for this reason, this class of micropollutants attracts particular attention of regulators and researchers alike.

Pharmaceuticals are classified based on their therapeutic use: antibiotics, antimicrobials (penicillins), anti-inflammatories and analgesics (ketoprofen, diclofenac), antiulcer and antihistamine drugs (ranitidine and famotidine), anti-diabetics (sulfonylurea), anti-epileptic (carbamazepine), anti-anxiety/hypnotic agents (diazepam), lipid regulators (Clofibrate), artificial steroid hormones (17-α-ethinylestradiol), to name a few (TIJANI, FATOBA, *et al.*, 2016). As availability and affordability of medicines across the world is increasing, in addition to population growth, population ageing (in some countries) and a widening array of medical treatments available, the use and environmental prevalence of phamaceuticals also increases on an annual basis, because a large proportion of these compounds cannot be assimilated and metabolized by the human body. They are therefore excreted via feces and urine and enter into municipal wastewater[2] treatment plants (COMBER, GARDNER, *et al.*, 2018, TIWARI, SELLAMUTHU, *et al.*, 2017). Pharmaceuticals have been detected in water bodies throughout the world, even in Antarctic Waters (PÉREZ-LEMUS, LÓPEZ-SERNA, *et al.*, 2019).

The primary sources of pharmaceutical pollutants in the environment are hospital and domestic wastewaters making up municipal wastewaters, though pharmaceutical industries, healthcare clinics, research activities utilizing therapeutic compounds and discharge of expired medicine in the environment also play a role in their dissemination. These compounds are partially metabolized and excreted in the urine and feces and go into a wastewater collection system (IKEHATA, EL-DIN, *et al.*, 2008, LUO, Yunlong, GUO, *et al.*, 2014, TIWARI, SELLAMUTHU, *et al.*, 2017). Another major source is the

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[2] In this thesis the term "municipal wastewater" is used as a synonym of sewage because sewage, according to METCALF, EDDY, 2003, is an older term, in disuse. The terms domestic wastewater and sanitary wastewater are also considered synonymous.

disposal of sewage from intensive livestock farming sites and effluents from intensive aquaculture systems, where the use of veterinary drugs the use of veterinary drugs is routine. These places are equally important but restricted to specific areas of countries routine (BOTTONI, CAROLI, *et al.*, 2010). Pharmaceuticals and (human) metabolites are degraded completely or partially by conventional wastewater treatment plants (WWTP), generating to a mixture of parent compounds, human and microbial metabolites that are released to surface water and may be subjected to groundwater recharges. Either way, the mixture of compounds enters the aquatic environment (THIEBAULT, BOUSSAFIR, *et al.*, 2017, TIJANI, FATOBA, *et al.*, 2016, TIWARI, SELLAMUTHU, *et al.*, 2017).

Nowadays, pharmaceuticals are widely detected in different environmental matrices such as surface water, soil, sediment, sludge and even drinking waters in some countries (COMBER, GARDNER, *et al.*, 2018). Pharmaceuticals in groundwater and sea coastal water have been detected as well (BOTTONI, CAROLI, *et al.*, 2010). Pharmaceuticals are micropollutants, so their concentrations in these matrices are also in the ug.L^{-1}-ng.L^{-1} range, but in the particular case of these compounds, authors have been reporting a direct relationship between the amount of drugs consumed by a given population and the concentration of pharmaceuticals found in receiving water bodies (COMBER, GARDNER, *et al.*, 2018, OOSTERHUIS, SACHER, *et al.*, 2013). Thus, data and patterns of drug use by a population become factors of interest in the selection of pharmaceuticals for environmental monitoring.

Chromatographic methods for pharmaceuticals detection

Several methods have been developed for the determination of pharmaceuticals in environmental matrices. These methods are primarily based on the use of gas or liquid chromatography (GC or LC) coupled with different types of detectors, for example fluorescence, diode array and the widely used mass spectrometry (MS) (FERNÁNDEZ-RAMOS, ŠATÍNSKÝ, *et al.*, 2014). GC–MS, LC–MS, high-performance liquid chromatography–diode array detector (HPLC–DAD) and comprehensive two-dimensional gas chromatography (GC × GC) are some of the most used chromatographic methods for pharmaceutical determination in environmental matrices (AKVAN, PARASTAR, 2014).

Pharmaceuticals are mostly polar compounds with limitations of volatility and/or thermal stability which prevent their analysis by GC directly; a prior derivatization step is necessary to increase the volatility of the compounds. Commmon derivatization processes include acylation (acetylation), alkylation and silylation. Although GC is a relatively cheap and efficient method, there has been a decline in its use for pharmaceuticals in favor of LC-based instrumental analysis, which account for about 73% of all analyzes of PhACs in environmental matrices (PÉREZ-LEMUS, LÓPEZ-SERNA, *et al.*, 2019). This is probably because LC is more versatile as a high number of compounds can be readily analyzes with no prior derivatization. A breakthrough in the LC method consists of High-Pressure Liquid Chromatography, where solvents, buffer and other mobile phases are pumped into the stationary phase by the high-pressure infusion system (PÉREZ-LEMUS, LÓPEZ-SERNA, *et al.*, 2019, ZHANG, Yan, QIAO, *et al.*, 2020). HPLC is suitable for detection of PhAcs with poor thermal stability has the advantages of high separation efficiency, improved selectivity, and fast analysis. It can be combined with UV, fluorescence, MS, and conductivity detectors, though the sensitivity of such detectors are not as good as that of GC (ZHANG, Yan, QIAO, *et al.*, 2020).

Environmental samples are complex and the qualitative and quantitative analysis of pharmaceuticals in trace amounts is challenging because of low selectivity and sensitivity of the entire analytical procedures (AKVAN, PARASTAR, 2014). Therefore, there is a need to includ an extraction step before chromatographic separation to 1) extract the analytes from complex sample matrices, reducing the complexity of the matrix; 2) eliminate interferences; 3) improve sensitivity; 4) reduce detection limit and 5) concentrate the analyte that occurs in the matrix in trace concentrations. Solid-phase extraction (SPE) and liquid-liquid extraction (LLE) are two of the most commom methods used as pretreatment (FERNÁNDEZ-LÓPEZ, GUILLÉN-NAVARRO, *et al.*, 2016, ZHANG, Yan, QIAO, *et al.*, 2020). Generally, preconcentration methods for PhAcs envolve SPE cartidges and a large variety of particle-extraction sorbents of different are currently available, but the Oasis HLB from Waters (provides lipophilic (divinylbenzene rings) and hydrophilic (Nvinylpyrrolidone) groups for the retention of non-polar and polar compounds) and the Strata-X material from Phenomenex (provides similar sorption properties via a polydivinylbenzene resin containing piperidone groups) have most often been used as extraction columns (FERNÁNDEZ-RAMOS, ŠATÍNSKÝ, *et al.*, 2014).

Criteria for selection of environmentally relevant compounds

It is important to discuss how to select phamaceuticals for analysis in environmental matrices, since there are more than 1,000 coumpounds that are synthesized and consumed on a regular basis and may, therefore, be expected at some degree to be present in the environment (ALONSO, EL KORI, *et al.*, 2018). It is clear no researcher can consider this amount. A rigorous selection of which pharmaceuticals should be selected, while ensuring representativeness, must be made, but the starting point for this selection is usually the environmental legislation, which however do not yet exist specifically for this class of micropollutants, with the exception of Switzerland (SILVA, Jessica Rodrigues Pires da, BORGES, *et al.*, 2020).

In the absence of regulations, some authors have dedicated themselves specifically to proposing pharmaceuticals selection methodologies, see (AL AUKIDY, VERLICCHI, *et al.*, 2014, DE VOOGT, JANEX-HABIBI, *et al.*, 2009, POCHODYLO, HELBLING, 2017). In addition, Table 1 presents a review of methodologies to select pharmaceuticals used by authors to select pharmaceuticals of interest in their studies.

Table 1: A review of methodologies found in literature to select pharmaceuticals for environmental studies.

Matrix	**PhACs analyzed**	**Methodology to select PhACs**	**Reference**
Synthetic municipal wastewater	Diclofenac, Ibuprofen, Naproxen, Carbamazepine, Dilatin, Primidone,Amitriptyline, Fluoxetine, Bezafibrate, Gemfibrozil, Sulfamethoxazole, Trimethoprim, Atenolol, Caffeine, Diphenhydramine, Iopromide, Benzophenone	Not presented	(WEI, WANG, *et al.*, 2018)
Synthetic municipal wastewater	Caffeine, atenolol , metoprolol , amoxicilin, trimethoprim, sulfadimidine, sulfamethoxazole, norfloxacin, ofloxacin, ciprofloxacin, lomefloxacin, enrofloxacin, oxytetracycline, tetracycline, chlortetracycline, doxycycline, clarithromycin, erythromycin, roxithromycin, azithromycin, carbamazepine, benzhabeite, estrone, estradiol , estriol	MPs that are found in wastewater and natural Waters and compounds´ physical-chemical characteristics.	(WANG, Yonggang, WANG, *et al.*, 2018)
Synthetic generic high strength wastewater	Carbamazepine, diclofenac and DEET	Not presented	(BOONNORAT, TECHKARNJANARUK, *et al.*, 2018)

Municipal wastewater	Galaxolide , gabapentin , carbamazepine and its metabolite carbamazepinedihydro-dihydroxy, diclofenac and its metabolite 4-hydroxy-diclofenac , metformin, tmetoprolol, sotalol, clarithromycin and sulfamethoxazole	Not presented	(BRUNSCH, TER LAAK, *et al.*, 2018)
Municipal wastewater previously treated by biological treatment	Atenolol, Bisoprolol, Bupropion, Carbamazepine, Citalopram, Clarithromycin, Clindamycin, Codeine, Diclofenac, Diltiazem, Fexofenadine, Flecainide, Fluconazole, Irbesartan, memantine, metoprolol, mirtazepine, oxazepam, sotalol, tramadol, trimethoprim, venlafaxine	Selection started over 100 substances that has shown high potency and potential for bioaccumulation in fish, and was narrowed to the 22 of higher occurence at the local wastewater treatment plant	(KÅRELID, LARSSON, *et al.*, 2017)
Black water or urine	Ibuprofen, diclofenac, paracetamol, trimethoprim, metoprolol and carbamazepine, estrone , estradiol and ethinylestradiol	Representant of different therapeutic groups, are widely used in large quantities in Europe and North America.	(DE WILT, BUTKOVSKYI, *et al.*, 2016)
Synthetic wastewater	Salicylic acid, naproxen, metronidazole, ibuprofen, primidone, diclofenac, gemfibrozil, carbamazepine,	PhACs selected to represent four major groups	(LUO, Wenhai, PHAN, *et al.*, 2017)

	DEET, estriol, Amitriptyline, benzophenone, oxybenzone, estrone, ethinylestradiol, estradiol, triclosan, ß-Estradiol-17-acetate	of micropollutants - that occur ubiquitously in municipal wastewater — endocrine disrupting compounds, pharmaceutical and personal care products, industrial chemicals, and pesticides.	
Municipal wastewater previously treated by biological treatment	Ketoprofen, naproxen, paracetamol, ibuprofen, diclofenac, sulfamethoxazole, ofloxacin, ciprofloxacin, trimethoprim, metronidazole, roxithromycin, norfloxacin, erythromycin, sulfadimerazine, sulfadiazine, sulfameter, sulfathiazole, atenolol, propranolol, carbamazepine, oxazepam, lorazepam, bezafibrate, fenofibrate, estrone, testosterone	Not presented	(MAILLER, GASPERI, *et al.*, 2014)
Municipal wastewater previously treated by activated sludge	Cefotaxime , Diatrizoate, Fenofibrate, Loratidine, Ketorolac , Traseolide, Urbason, Paroxethine, Fenoprofen, Erythromycin, Terbutaline, Amitriptyline, Antipyrine Azithromycin ,	First screen was for 77 PhACs, no criteria presented. Second screen was the 12 compounds of the first	(URTIAGA, PÉREZ, *et al.*, 2013)

	Citalopram , Clomipramine, Ifosfamide, Iopamidol, Iopromide, lincomycin, Sulfamethazine ,Nadolol , Fluoxethine, 4-Dimethylaminoantipyrine (4-DAA), 4 MMA, acetaminophen, atenolol, bezafibrate, caffeine, carbamazepine, ciprofloxacin, codeine, diazepam, fluoxetine, furosemide, gemfibrozil , Hydrochlorothiazide, ibuprofen, indometachin, ketoprofen, mepivacaine, metoprolol, metronidazole, N-Acetyl-4-amino-antiyirine (4-AAA), N-Formyl-4-amino- antiyirine (4-FAA), nicotine, naproxen, ofloxacin, omeprazole, paraxanthine, propranolol, ranitidine, salbutamol, sotalol, sulfamethoxazole, trimethoprim, clarithromycin, cotinine, phenacetin, pravastatin, salicylic acid, sulfapyridine , benzophenone 3, celestolide, Ethylhexyl methoxycinnamate, galaxolide, triclosan, Tonalide, octocrylene, Traseolide	screen that had the highest concentrations for each therapeutic category.	
Synthetic wastewater and raw sewage	Amitriptyline, diclofenac, carbamazepine, sulfamethoxazoole, caffeine, trimetoprim, primidone, bezafibrate	PhACs selected to cover a diverse range of properties, including charge, volatility,	(XIE, NGHIEM, *et al.*, 2013)

		hydrophobicity, and molecular weight. Also, MPs were selected are frequently detected in raw sewage.	
Municipal wastewater previously treated by activated sludge	Acetaminophen, 4-Aminoantipyrine, atorvastatin, bezafibrate, ciprofloxacin , clarithromycin, clindamycin, diclofenac, enalapril, erithromycin, gemfibrozil, ibuprofen, ketoprofen, lincomycin, lorazepam, naproxen, ofloxacin, salycilic acid, sulfamethoxazole, venlafaxine, valsartan, irbesatan, furosemide, carbamzepine, gabapentin	Not clearly presented. Mentions target PhACs were updated considering 5 pharmaceuticals widely detected in wastewaters of the area (out of a total of 52)	(IBÁÑEZ, GRACIA-LOR, *et al.*, 2013)
Synthetic wastewater	Salicylic acid, parcetamol, DEET, caffeine, simazine, ibuprofen, primidone, naproxen, carbamazepine, gemfibrozil, dilantin, sulfametoxazole, ketoprofen, atenolol, estrone, estradiol, Amtriptyline, Androstenedione, Estriol, Testosterone, Triclosan, Trimethoprim, Etiocholanolone, Androsterone , Diclofenac. 17a-Ethynylestradiol, Fluoxetine, Triclocarban,	Fifty PhACs selected to represent four major groups of concern in water reuse applications – pharmaceutically active compounds, pesticides, steroid hormones and other endocrine disrupting chemical. Moreover,	(ALTURKI, Abdulhakeem, MCDONALD, *et al.*, 2012a)

	Clozapine, Omeprazole, Hydroxyzine, Enalapril, Risperidone, Simvastatin, Methotrexate , Verapamil	mentioned many of these 50 PhACs have been widely reported in the literature in domestic sewage.	
Synthetic wastewater	Triclosan and diclofenac	PhACs selected because they are ubiquitous trace organic contaminants in secondary treated effluent and non-potable recycled water. Moreover, their physicochemical properties were essential in their choice, as authors wanted to provide variable 'solute-membrane' interactions and subsequent removal behaviour.	(XIE, NGHIEM, *et al.*, 2012)
Reverse osmosis retentate from municipal wastewater	Gemfibrozil, naproxen, carbamazepine, ofloxacin, erythromycin, trimethoprm, venlafaxine, atenolol, metoprolol, caffeine, nalidix acid, iohexol, DEET,	PhACs frequently detected in wastewaters effluents	(ABDELMELEK, GREAVES, *et al.*, 2011)

previously treated by activated sludge	sulfamethoxazole, atorvastatin, lovastatin, enrofloxacin, sulfamethazine, sulfamethizole, sulfamerazine, cimitidine, farnotidine, ranitidine, iopamidol, iomeprol, iopromide		
Surface and groundwater used for drinking purposes	Surface water: cholesterol, cotinine (nicotine metabolite) and 1,7-dimethylxanthine (caffeine metabolite). Grondwater: carbamazepine, bisphenol-A, 1,7-dimethylxanthine (caffeine metabolite)	Known or suspected usage, toxicity, potential hormonal activity, persistence in the environment, as well as results from previous studies.	(FOCAZIO, KOLPIN, *et al.*, 2008)
Hospital wastewater and municipal wastewater	Hospital wastewater: Acetaminophen, caffeine, gabapentin, ibuprofen, metformin, naproxen, theobromine and theophylline. Municipal wastewater: acetaminophen, caffeine, furosemide, gabapentin, metformin, sulfamethoxazole, theobromine and trimethoprim	USEPA Method 1694 and a list of most prescribed drugs in the USA	(OLIVEIRA, MURPHY, *et al.*, 2015)
Raw drinking water and municipal wastewater	Raw drinking water: carbamazepine, gabapentin, primidone, acetaminophen, norfloxacin. Municipal wastewater: ibuprofen, acetaminophen, carbamazepine, gabapentin, benzafibrate, iohexol,	Annual sales volumes of pharmaceuticals (as far as available), the degree of human metabolization and the estimated removal in the	(MORASCH, BONVIN, *et al.*, 2010)

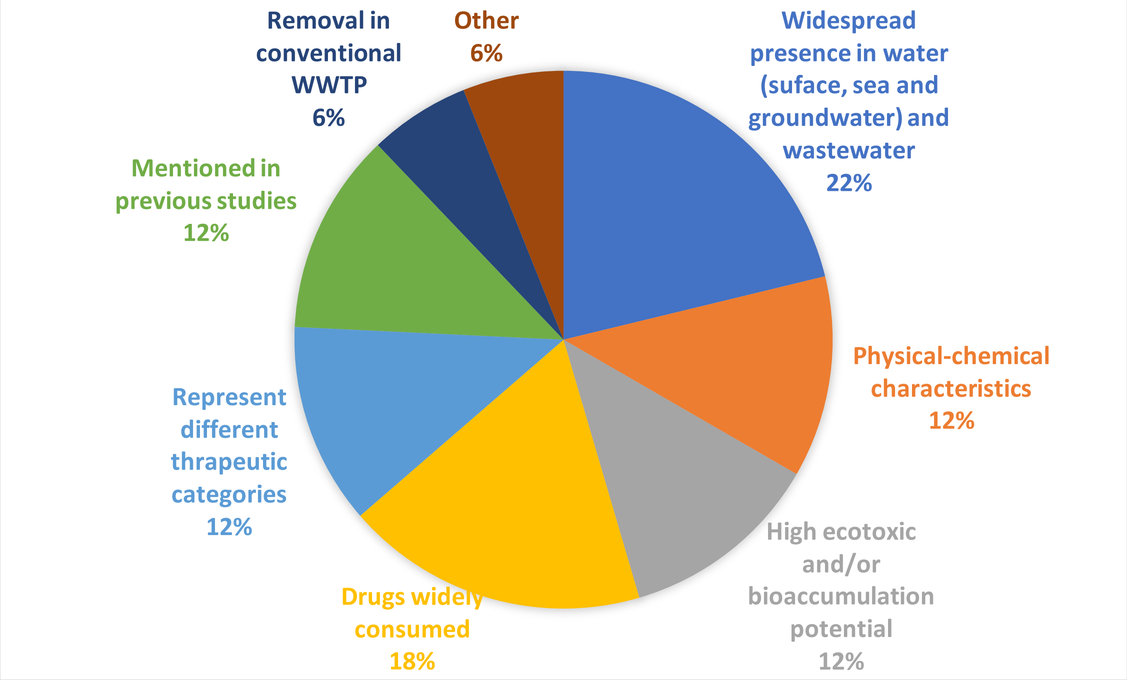
	iomeprol, iopromide, benzotriazole, methylbenzotriazole.	WWTP, presence in previous monitoring campaigns, direct request from the Swiss Federal Office for the Environment.	
Municipal wastewater	Acesulfane, sucralose, benzotriazoles, carbamazepine, tramadol, telmisartan, venlafaxine, irbesartan, fluconazole, oxazepam, fexofenadine, diclofenac, citalopram, codeine, bisoprolol, eprosartan, trimethoprim, ciprofloxacine, sulfamethoxazole, clindamycine, caffeine.	Not presented	(LOOS, CARVALHO, *et al.*, 2013)
Seawater	>50% samples: Caffeine, paraxanthine, theobromine, tolyltriazole, 1H-benzotriazole, carbamazepine, iopamidol, sulfamethoxazole, paracetamol, theophylline and atenolol	Not presented	(NÖDLER, VOUTSA, *et al.*, 2014)
Hospital wastewater and municipal wastewater (including hospital and domestic)	Acetaminophen, flecainide, fluconazole, ciprofloxacin, ofloxacin, levofloxacin, sulfamethoxazole, trimethoprim and progesterone	Not presented	(LINDBERG, ÖSTMAN, *et al.*, 2014)

Surface and groundwater	>70% samples: salicylic acid (metabolic of aspirin), carbamazepine; acetaminophen; diclofenac; sulfamethoxazole, testosterone, androstenedione and progesterone	Consumption by french population, predicted by environmental concentrations as well as ecotoxicological, pharmacological and physicochemical data	(VULLIET, CREN-OLIVÉ, 2011)
Surface water	Caffeine, acetaminophen, Atenolol, Ibuprofen, Naproxen, Diclofenac, Triclosan, propanolol, Carbamazepine	For caffeine, results from previous studies. For the rest, not presented	(CAMPANHA, AWAN, *et al.*, 2015)
Municipal wastewater	Paracetamol, hydrochlorothiazide, furosemide, naproxen, ibuprofen, diclofenac, bezafibrate, gemfibrozil, simvastatin, ketoprofen, azithromycin, bisoprolol, lorazepam and paroxetine	Environmental relevance	(SOUSA, GONÇALVES, *et al.*, 2011)
Municipal wastewater	Ibuprofen, acetaminophen, ofloxacin, gemfibrozil, bezafibrate, atenolol, glibenclamide, hydrochlorothiazide	Not presented	(RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)
Municipal wastewater	Paracetamol, caffeine, trimethoprim, sulfamethoxazole, carbamazepine, diclofenac and salicylic acid	High annual consumption, previous studies about their occurrence, removal in	(KOSMA, LAMBROPOULOU, *et al.*, 2014)

		wastewaters and surface waters, stability and poor elimination during wastewater treatment and concern about their possible effects on human and aquatic life	
Municipal wastewater	4-Aminoantipyrine, bezafibrate, diclofenac, gemfibrozil, ketoprofen, naproxen and venlafaxine	Special focus to antibiotics because of the possible promotion of bacterial resistance	(GRACIA-LOR, SANCHO, *et al.*, 2012)

Figure 2 shows the percentage of use of each criteria mentioned in Table 1. Each study can present one or more criteria at the same time.

Figure 2: Pie chart illustrating the percentage of use of each selection criterion considering the studies selected in Table 1.



The most commonly used criteria to select a pharmaceutical is its widespread presence in water (suface, sea and groundwater), however, it is noteworthy that 8 articles, which correspond to 31% of the total in Table 2, do not mention any selection criteria. A critical discussion of these criteria and their implications for the representativeness of selection, including possible bias, is given in detail in the article "A Critical Review of Criteria Used For the Selection of Pharmaceuticals and Personal Care Products in Different Environmental Matrices"[3] published by the author.

Environmental and health concerns associated with ocurrence of pharmaceuticals

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[3] "A Critical Review of Criteria Used For the Selection of Pharmaceuticals and Personal Care Products in Different Environmental Matrices", article published in Environmental Pollution and Protection, Vol. 5, No. 1, March 2020, https://dx.doi.org/10.22606/epp.2020.51002

Pharmaceuticals, unlike most other chemical compounds that enter the environment, are designed to alter physiological functions in order to achieve specific therapeutic effects. Therefore there is a high probability of them being biologically active towards wildlife species as well (LINDIM, DE ZWART, *et al.*, 2019, VASQUEZ, LAMBRIANIDES, *et al.*, 2014). Some of the adverse effects expected may include disruptions of endocrine system, chronic toxicity and increase in PhAC resistant bacterial strains (TIJANI, FATOBA, *et al.*, 2016). These adverse effects have become apparent by a number of publications.

For example, a study by KIDD, BLANCHFIELD, *et al.*, 2007 assessed chronic exposure of fathead minnow (*Pimephales promelas*) to low concentrations (5–6 ng.L^{-1}) of synthetic steroid hormone 17α-ethynylestradiol over 7 years in a lake, demonstrating feminization of males and impacts on gonadal development as evidenced by intersex in males and altered oogenesis in females, ultimately leaving population of this species from the lake near extinction. This study demonstrated that even very low concentrations of estrogens in water can impact the sustainability of wild fish populations. Vázquez et al. 2014 reported that, at environmentally relevant concentrations, antibiotics inhibite growth on a variety of ecotoxic organisms, influence biolumiscence and biodegradation performances; antidepressants affect secondary sex characteristics of fathead minnow; mixture of anti-infflamatory and antibiotics affects growth, reproduction, protein expression profile, mobility, diversity and morphology of a variety of organisms, and so on. GODOY, KUMMROW, *et al.*, 2015 in a similar review also reported pharmaceuticals (mostly antihypertensives) in mixtures at environmentally relevant concentrations increased body length of Daphnia magna overy various generations; created inflammatory mechanisms in *Lymnae stagnalis*; had endocrine disrupting effects in D. rerio and *R.subcapitata*; and affected chloropast of algae.

The most frequently detected pharmaceutical compounds in the environment fall within the classes of analgesics, antibiotics, diuretics, beta-blockers, hormones, antidepressants, psychiatric, hormones, and lipid regulators (VASQUEZ, LAMBRIANIDES, *et al.*, 2014). The class of antibiotics is one that causes much concern because of influence of trace antibiotics on the spread of microbial resistance genes in the environment, which is now is widely recognized; several authors report decisive results linking wastewater treatment plants (WWTP) with the development and dissemination of antibiotic resistance genes (ARGs) (GALLER, FEIERL, *et al.*, 2018, LÉPESOVÁ, KRAKOVÁ, *et al.*, 2018). Another class of great concern is that of endocrine disruptors. Endocrine systems regulate the body's physiological activities such as reproductive functions, but its has been found that certain micropollutants including some pharmaceuticals can mimic or disrupt endocrine glands from functioning properly (Tijani et al. 2016). Effects are observed in the form of alteration of chemical messengers of the body or binding to receptors of the endocrine system, that are responsible for development, behaviour, fertility, and maintenance of homoeostasis (normal cell metabolism) (TIJANI, FATOBA, *et al.*, 2016). Consequences may lead to intersex alterations, which have been observed in among alligators, frogs and fish. Recognized endocrine disrupting compounds include phthalates, phenolic compounds (bisphenol-A, nitrophenol, nonylphenol, alkylphenol, and chlorophenols), triclosan, 17-α-ethinylestradiol, diethylstilbestrol and 17β-estradiol (KIDD, K. A., BLANCHFIELD, *et al.*, 2007, TIJANI, FATOBA, *et al.*, 2016, TOMPSETT, WISEMAN, *et al.*, 2013).

A recent study (LINDIM, DE ZWART, *et al.*, 2019) has pointed that chronic effects to aquatic wildlife are predominantly caused by paracetamol, diclofenac (anti-inflammatories), ethinylestradiol (estrogen), erythromycin and ciprofloxacin (antibiotics). Diclofenac residues were directly correlated with reinal failure in vulture, a typical bird from the Indian continent that has gained notoriety in the scientific community when a decline of more than 90% in its population in less than a decade was discovered. A study published in Nature journal proposed that these diclofenac residues were directly responsible for the population's decline (OAKS, GILBERT, *et al.*, 2004).

Adverse effects on the environment are usually assessed on aquatic life by tests on organisms typically used in ecotoxicity tests such as algae, crustaceans, fishes (PASQUINI, MERLIN, *et al.*, 2013). Research regarding exposure and effects in non-target higher vertebrates remains scarce, however, growing in attention because of possible biomagnification along food chains (SHORE, TAGGART, *et al.*, 2014). Besides the aforementioned effect of diclofenac on vultures, adult male starlings (Sturnus vulgaris) experimentally exposed to environmentally relevant levels of various endocrine disruptor compounds displayed altered immune function and changed development that affected behaviours such as singing (SHORE, TAGGART, *et al.*, 2014). For the PhACs selected in the present study, a compilation of available toxicological data for assays in environmental relevant concentrations (ng.L^{-1} - µg.L^{-1}) is presented in the Appendix of this Chapter.

It should be noted that in spite of these well established effects on wildlife, some scientists have reported that the risk to public health might be minimal because human beings are being exposed to micropollutants in water at extremely trace levels compared to the exposure to these compounds present in food sources or by direct, ocasional ingestion (YANG, ZHOU, *et al.*, 2014). The World Health Organization (WHO) issued a document in this matter in 2012 stating "[...] adverse human health impacts are very unlikely from exposure to pharmaceuticals that could pottentially be found in treated drinking-water", as risk assessments from regulatory agencies from United Kingdom, the US and Australia, corroborated by scientific literature showed that for pharmaceuticals that have been detected in drinking water, the concentrations are more than 1000-fold less than the minimum therapeutic dose i.e. the lowest clinically active dosage (WORLD HEALTH ORGANIZATION, 2011). This matter, though, is still subject to research.

2.2.2 Activated sludge

Process fundamentals

Biological processes are considered the most economical choice and one of the most environmentally suitable options for wastewater treatment, because through the metabolic capabilities of microorganisms they are efficient in removing organic matter and some pathogens such as coliforms at a relative low cost (ADISHKUMAR, SIVAJOTHI, *et al.*, 2012). For these reasons, they are in most cases the standard choice for the treatment of municipal and industrial wastewater. Activated sludge (AS), in particular, stands out among aerobic biological systems. Most of WWTP treating urban municipal wastewater employ this process, which allows satisfactory removal of classical chemical parameters such as Biological Oxygen Demand (BOD) (PASQUINI, MERLIN, *et al.*, 2013, THIEBAULT, BOUSSAFIR, *et al.*, 2017)

Activated sludge is a specialized, aerobically-grown culture containing flocculated and non-flocculated microorganisms such as bacteria, protozoa (ciliates, flagellates, amoebae), metazoa (rotifers, nematodes) and fungi forming a complex relationship within the activated sludge community. Bacteria, in particular heterotrophic bacteria aggregated in flocs and freely dispersed, form the largest group of microorganisms, and they are mostly gram-negative, non-fermentative and oxidase-positive members of genera such as Pseudomonas, Bacillus, Micrococcus, Flavobacterium, Achromobacter, and Zooglea, all belonging to phylum Proteobacteria This bacterial phylum can be regarded as the main group responsible for pollutant removal (SOWINSKA, PAWLAK, *et al.*, 2017, VÁZQUEZ-RODRÍGUEZ, BELTRÁN-HERNÁNDEZ, *et al.*, 2011). Moreover, activated sludge flocs are of paramount importance as they are directly related to the stability of biodegradation process. Hydrodynamic conditions (mixing of reactor) and oxygen supply influence the shape, size and distribution of the flocs. Appropriate conditions make the flocs evenly distributed in their size and with a specific shape (VUKOVIĆ DOMANOVAC, ŠABIĆ RUNJAVEC, *et al.*, 2019). This is essential for a good setteability of the flocs, allowing obtaining good quality treated wastewater.

The activated sludge process provides two pathways for the removal of BOD, (1) oxidation of organics to provide energy for the metabolic processes of the microorganisms, which correspond to approximately 40% of input carbon, and (2) incorporation of the organic matter into cell mass or for production of new cells, which correspond to approximately 60% of input carbon. In the first pathway, carbon is removed in the gaseous form as CO_2 and so it does not present a disposal problem, unlike the second pathway, because as new cells (biomass) are formed, their excess will eventually need to be disposed as waste (MANAHAN 2000). The need to manage this sludge waste creates an additional operational cost and consists, along with electrical cost of aerating the system, the two drawbacks of this process. Overall, activated sludge is considered the most versatile and effective of all wastewater treatment processes for sewage (MANAHAN 2000).

Acclimatization

Microorganisms are able to develop mechanisms of resistance and metabolism once exposed to novel environmental pollutants or environmental perturbations. This exposition may lead to the development of novel enzymes and even novel catabolic pathways (POURSAT, VAN SPANNING, *et al.*, 2020). A well known example is the development of resistance mechanisms to antibiotics in the natural environment by bacterial species (UHLEMANN, 2019). In respect to biodegradation, acclimatization[4] is a term that defines deliberate pre-exposure of microorganisms in a inoculum to a chemical or mixture of chemicals (POURSAT, VAN SPANNING, *et al.*, 2020). The indigenous microbial population can degrade newly introduced toxic or recalcitrant compounds only after going through an acclimation process, observing a period of dormant time (lag-phase) during which this population is placed in reaction with the compound and undergoes a series of enzyme induction processes, resulting in biochemical changes to initiate the biodegradation of the specific substrate (CHONG, 2009, POURSAT, VAN SPANNING, *et al.*, 2020).

Therefore, acclimatization results in the adaptation of the microorganisms to its new operational conditions, where sludge microbes develop natural resistance to variations in such conditions, avoiding inhibition of sludge biological activity. A sucessful acclimatization may reduce the lag-phase, which is which is thetime required for a community to start degrading a compound (POURSAT, VAN SPANNING, *et al.*, 2020) or even allow degradation of toxic chemicals. In these cases, members of the community can increasingly withstand the potential toxic effects of chemicals and eventually degrade them through adaptation and evolution both at a community and individual cell level (POURSAT, VAN SPANNING, *et al.*, 2020).

Whenever a biological system is subjected to a disturbance in the environment (for example by changing the characteristics of the feed wastewater) or the introduction of new potentially toxic and / or non-biodegradable compounds, an acclimatization step is necessary. Despite its importance, there are no standardized procedure for acclimating inocula exists (ELÍAS, BARONA, *et al.*, 2010) and some authors research more appropriate methods depending on the biological system (ELÍAS, BARONA, *et al.*, 2010, FERRER-POLONIO, MENDOZA-ROCA, *et al.*, 2015).

Regarding PhACs, literature results on whether the existence of an acclimatization stage interferes with efficiency of their removal are contradictory: PHAN, HAI, *et al.*,

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[4] Acclimatization and acclimation are used interchangeably in literature, i.e. they are synonyms.

2016 found MP induce shifts in bacterial communities, and that there is a correlation between these communities and MP biotransformation whereas ALIDINA, LI, *et al.*, 2014, FALÅS, WICK, *et al.*, 2016 did not.

Moreover, most studies that investigate the effects and relationships of the MPs with biological process focus on alterations in microbial community profile and gene expressions (AMORIM, ALVES, *et al.*, 2018, HARB, WEI, *et al.*, 2016a, KRUGLOVA, GONZALEZ-MARTINEZ, *et al.*, 2017). A very limited number of studies (LIWARSKA-BIZUKOJC, GALAMON, *et al.*, 2018) evaluated the effects created by the introduction of low concentration of MPs in terms of process performance, which constitutes a gap in the literature that was addressed by this Thesis.

Pharmaceutical removal

Overall, pharmaceutical removal efficiency by biological processes depends on the treatment process, physicochemical properties of these organic compounds, microbial populations, operational parameters such as pH, temperature, sludge retention time, biomass concentration, hydraulic retention time, redox conditions, heterotrophic activity and suspended/attached growth (FALÅS, WICK, *et al.*, 2016, KANAKARAJU, GLASS, *et al.*, 2018). Key PhAC removal mechanisms are biotic (biodegration/transformation) or abiotic (volatilization/stripping by aeration, isomerisation/epimerisation, hydrolytic degradation, sorption on solids and photodegradations (LOOS, CARVALHO, *et al.*, 2013, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009).

Most MPs have a low value of Henry Law constant, and so volatilization is not considered and important removal mechanism. Sorption on solids, on the other hand, are particularly important when the affinity of compounds to be retained onto sludges is high; measure of sorption quantities require the solid water distribution coeficientt (k_d) (NSENGA KUMWIMBA, MENG, 2019). Note that the disappearance from the aqueous phase does not necessarily mean the disappearance of the compost, but perhaps the transfer of medium to sludge or else conversion to other compounds (i.e. intermediates). In the case of transfer to sludge, MP can still enter the environment if not properly treated and applied to the farmland, for example (IBÁÑEZ, GRACIA-LOR, *et al.*, 2013, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009). In turn, photodegradation is suggested to be a very relevant removal pathway of some MP in natural systems only.

The majority of MPs in WWTP is thus regarded as removed by biodegradation, which can be enhanced by higher mixed liquor suspended solids concentration. Biodegradation pathways include metabolism and/or cometabolism (NSENGA KUMWIMBA, MENG, 2019). Co-metabolism is the process where organic compounds (such as MPs) can be metabolized by microorganisms in the presence of a primary substrate that serves as the main energy and/or carbon source, and which is not the MP. Degradation is this case is caused by the enzyme or cofactor produced during microbial utilization of primary substrates, rather than the presence of the organic compounds (such as MPs) themselves (ALIDINA, LI, *et al.*, 2014). In metabolisms, mciroorganisms use directly the MPs as the sole energy and/or carbon source to sustain their biomass and produce relevant enzymes for oxidation/reduction. Co-metabolism is considered the main pathway for most MP elimination (ALIDINA, LI, *et al.*, 2014, NSENGA KUMWIMBA, MENG, 2019).

A full understanding of the interactions between all the variables in the biological process is still lacking, however, it is recognized that organic micropollutants can generally be divided into easily, moderately and poorly degradable compounds in conventional biological wastewater treatment systems, whatever the plant studied (FALÅS, WICK, *et al.*, 2016, THIEBAULT, BOUSSAFIR, *et al.*, 2017) and illustrated in Table 2. Those who belong to sporadically or poorly degradable grups should therefore be prioritized in advanced treatment systems to reach or maintain low residual concentrations in biologically treated wastewater, thus avoiding or reducing these compounds in receptor water bodies (FALÅS, WICK, *et al.*, 2016).

Table 2: A review of removal of selected pharmaceuticals by conventional WWPTs (activated sludge treating municipal wastewater) in different countries.

Therapeutic category	**Pharmaceutical**	**Sampling sites**	**Removal (%)**	**Reference**
Antiobiotic	Sulfamethoxazole	United Kingdom, Spain, Switzerland, Germany, Saudi Arabia, Taiwan	0-98	(AL QARNI, COLLIER, *et al.*, 2016, FALÅS, WICK, *et al.*, 2016, KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, LIN, LIN, *et al.*, 2010, MARTÍN, CAMACHO-MUÑOZ, *et al.*, 2012, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)
	Trimethoprim	United Kingdom, Spain, Switzerland, Germany	0-74	(FALÅS, WICK, *et al.*, 2016, KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, MARTÍN, CAMACHO-MUÑOZ, *et al.*, 2012, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)
	Erythromycin	United Kingdom, Spain, Taiwan	0-50	(KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, LIN, LIN, *et al.*, 2010, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)
Anti-epilectic	Carbamazepine	United Kingdom, Spain, Switzerland, Germany	0-50	(FALÅS, WICK, *et al.*, 2016, KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, MARTÍN, CAMACHO-MUÑOZ, *et al.*, 2012, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)

β-blocker	Metoprolol	United Kingdom, Spain, Switzerland, Germany	25-56	(FALÅS, WICK, *et al.*, 2016, KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)
	Atenolol	United Kingdom, Spain, Switzerland, Germany, Saudi Arabia	61-92	(AL QARNI, COLLIER, *et al.*, 2016, FALÅS, WICK, *et al.*, 2016, KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)
Nonsteroidal anti-inflammatory	Ibuprofen	United Kingdom, Spain, Taiwan, Sweden	50-99	(KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, LIN, LIN, *et al.*, 2010, MARTÍN, CAMACHO-MUÑOZ, *et al.*, 2012, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009, ZORITA, MÅRTENSSON, *et al.*, 2009)
	Naproxen	United Kingdom, Spain, Taiwan, Sweden	57-96	(KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, LIN, LIN, *et al.*, 2010, MARTÍN, CAMACHO-MUÑOZ, *et al.*, 2012, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009, ZORITA, MÅRTENSSON, *et al.*, 2009)
	Ketoprofen	United Kingdom, Spain, Taiwan	38-76	(KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, LIN, LIN, *et al.*, 2010, MARTÍN, CAMACHO-MUÑOZ, *et al.*, 2012, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009, ZORITA, MÅRTENSSON, *et al.*, 2009)

	Acetaminophen	United Kingdom, Spain, Switzerland, Germany, Saudi Arabia, Taiwan	98-100	(AL QARNI, COLLIER, *et al.*, 2016, FALÅS, WICK, *et al.*, 2016, KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, LIN, LIN, *et al.*, 2010, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)
	Diclofenac	United Kingdom, Spain, Taiwan, Sweden	0-42	(KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, LIN, LIN, *et al.*, 2010, MARTÍN, CAMACHO-MUÑOZ, *et al.*, 2012, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009, ZORITA, MÅRTENSSON, *et al.*, 2009)
Lipid regulator	Gemfibrozil	Spain	0-15	(MARTÍN, CAMACHO-MUÑOZ, *et al.*, 2012, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)
	Bezafibrate	United Kingdom, Spain, Switzerland, Germany	65-90	(FALÅS, WICK, *et al.*, 2016, KASPRZYK-HORDERN, DINSDALE, *et al.*, 2009, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009)
Steroidal hormone	Estrone	South Africa, Spain, Sweden, United Kingdom	0-93	(MARTÍN, CAMACHO-MUÑOZ, *et al.*, 2012, PETRIE, MCADAM, *et al.*, 2014, ZORITA, MÅRTENSSON, *et al.*, 2009)
	17-α-ethinylestradiol	South Africa, Spain, United Kingdom	29-90	(MANICKUM, JOHN, 2014, PETRIE, MCADAM, *et al.*, 2014, ZORITA, MÅRTENSSON, *et al.*, 2009)

Table 2 shows PhACs belonging to the same therapeutic group may demonstrate very differing removal rates, for example, acetaminophen[5], naproxen and diclofenac. It is also known that some PhACs conjugates such as glucoronides can be cleaved by microbial degradation resulting in a release of parent compounds in treated wastewaters, which may reduce removal rates and eventually even result in "negative" removal rates (IKEHATA, EL-DIN, *et al.*, 2008). The partially eliminated micropollutants (<90% efficiency removal) are likely to reach different environmental matrices (e.g., surface water, soil/sediment, drinking water and groundwater) all over the world. Considering the known risks to aquatic wildlife and the principle of pollution prevention, strategies for maximize their removal in both natural and engineered systems are potentially required (NSENGA KUMWIMBA, MENG, 2019).

2.2.3 Advanced Oxidation Processes

Definitions

Biological treatment is usually the most cost-effective technology for removal of organic matter of wastewater. Some organics, however, are either nonbiodegradable or toxic to the biological process, so they must be pre- or post-treated. Pre-treatment by chemical oxidation can alter detoxication and enhance biodegradation in many cases, and chemical post-oxidation may reduce the toxicity and the amount of organic recalcitrant material or biological by-products in wastewater (PARSONS 2004). Advances in chemical water and wastewater treatment have led to a range of processes termed advanced oxidation processes (AOP), which can be precisely defined as water treatment processes performed at room temperature and normal pressure and based on the *in situ* generation of a oxidizing agent, hydroxyl radical (•OH), at a sufficient concentration to effectively react with various organic and inorganic compounds (OTURAN, AARON, 2014).

Hydroxyl radicals (OH·) generated in these processes are defined by their non-selective nature, high reactivity and powerful oxidizing capabilities ($E^o = + 2.80$ V),

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[5] Acetaminophen can also be known in literature as paracetamol.

second only to fluorine (E^o = + 3.03 V) and therfore able to attack a wide range of organic contaminants, with rate constants normally in the order of 10^6-10^9 $M^{-1}s^{-1}$. They react with compounds through hydrogen abstraction, radical-radical reactions, electrophillic addition, and electron transfer reaction (KANAKARAJU, GLASS, *et al.*, 2018). They are therefore expected to readily degrade recalcitrant organic pollutants and remove certain inorganic pollutants in wastewater. Examples of AOPs include O_3/H_2O_2, O_3/UV, O_3/H_2O_2/UV, H_2O_2/UV, Fenton (Fe^{2+}/H_2O_2), photo- and electro-Fenton, chelating agent assisted Fenton/photo-Fenton, heterogeneous photooxidation using titanium dioxide (TiO_2/hn), g-radiolysis, and sonolysis (IKEHATA, EL-DIN, *et al.*, 2008, OTURAN, AARON, 2014). Although hydroxyl radical is the main oxidizing agent, their application often induces production of other reactive oxygen species (ROS) as well such as superoxide radical anions, hydroperoxyl radicals, singlet and triplet oxygen (GIANNAKIS, GAMARRA VIVES, *et al.*, 2015).

Mineralization, that is, the convertion of constituents of an organic pollutant into simple, relatively harmless and inorganic molecules, is the ultimate aim of the oxidation of pollutants in waters/wastewaters. This however is not always achievable, because once a free radical (hydroxyl) reaction has been initiated by photolysis, ozone, hydrogen peroxide, heat, etc a large number of reactions will follow in parallel, which creates a very complex chemistry in the medium that makes it difficult to achieve mineralization (PARSONS 2004). The degradation of dissolved organics in biologically treated effluents, for example, is recognized by many authors as very difficult to achieve (GIANNAKIS, GAMARRA VIVES, *et al.*, 2015, RODRÍGUEZ-CHUECA, LASKI, *et al.*, 2018, SARKAR, ALI, *et al.*, 2014, SILVA, Larissa L.S., SALES, *et al.*, 2017). In fact, during the application of AOPs, the main concern is related precisely to the formation of these various intermediate products formed as a consequence of the nonselectivity of hydroxyl radicals that trigger complex reaction pathways. Therefore, disappearance of the original pharmaceutical may not imply that the treatment alone is efficient because the degraded products may be as biologically active as the parent compounds(FATTA-KASSINOS, VASQUEZ, *et al.*, 2011, GOMES, GANDO-FERREIRA, *et al.*, 2018, IKEHATA, EL-DIN, *et al.*, 2008).

Parameters such as chemical oxygen demand (COD), dissolved organic carbon (DOC), absorbable organic halogene or aromaticity can be used as proxies to concomitantly to evaluate the effectiveness of the oxidation process, but they do not provide direct information about the identity of degradation products; for that, LC and/or GC analysis are necessary (FATTA-KASSINOS, VASQUEZ, *et al.*, 2011, IKEHATA, EL-DIN, *et al.*, 2008).

Overall, water matrix constituent have a major influence on removal of micropollutants and other organics, and this happens because 1) water matrix contains numerous non-target organic and inorganic species that compete with the target contaminants for oxidants and 2) water matrix has scavengers that reduce process efficiency; the most common in natural waters are NOM, bromide and carbonate/bicarbonate ions. Other compounds that may act as scavengers include carbohydrates, proteins, nitrite, sulfate and chloride. Scavengers hamper the process either by competing with organic MPs for oxidation or forming the respective radicals with lower oxidation potential. Besides interfering with the process performance, the water matrix may also influence the production and nature of the transformation by-products, for example, reactions in the presence of chlorides are prone to originate toxic chlorinated by-products (RIBEIRO, MOREIRA, *et al.*, 2019). These facts attest the need to consider water chemistry of paramount importance when selecting and discussing AOPs.

UV/ H_2O_2

Photochemical technologies present the advantages to be simple, clean, relatively inexpensive, and generally more efficient than chemical AOPs. As a result, ultraviolet (UV) irradiation and UV-based advanced oxidation processes AOPs have received considerable attention in the past decade for micropollutants removal from wastewater (KANAKARAJU, GLASS, *et al.*, 2018, OTURAN, AARON, 2014, YANG, ZHOU, *et al.*, 2014). UV is gaining wide application for microbial disinfection, but in addition to this property of inactivating microorganisms, UV can also degrade organic compounds by direct photolysis as a consequence of UV light absorption (i.e. UV direct photolysis) or by indirect processes assisted by the addition of oxidants such as hydrogen peroxide (H_2O_2) (YANG, ZHOU, *et al.*, 2014).

Hydrogen peroxide can be photolyzed by UV radiations absorbed at wavelengths ranging from 200 to 300 nm; the radiation yields homolytic scission of the O–O bond of the H_2O_2 molecule, leading to the formation of •OH radicals (Equation 1) that can also contribute to the decomposition of H_2O_2 by secondary reactions (Equatios 1 to 7) (OTURAN, AARON, 2014). Equation 1 corresponds to the initiation step, Equations 2 to 4 to the propagation steps, and Equations 5 to 7 to the termination steps.

Equation 1

$$H_2O_2 + hv \rightarrow HO\cdot\ + OH\cdot$$

Equation 2

$$HO\cdot\ + H_2O_2 \rightarrow H_2O + HO_2\cdot$$

Equation 3

$$HO_2\cdot\ + H_2O_2 \rightarrow\ HO\cdot\ + H_2O\ +\ O_2$$

Equation 4

$$HO\cdot\ + {HO_2}^{-}\ \rightarrow\ HO_2\cdot\ + OH^{-}$$

Equation 5

$$2HO_2\cdot \rightarrow H_2O_2 +\ O_2$$

Equation 6

$$HO\cdot\ + HO_2\cdot \rightarrow\ H_2O + O_2$$

Equation 7

$$HO\cdot \rightarrow\ H_2O_2$$

Low-pressure mercury vapor lamps with a 254-nm peak emission are the most common UV source used in UV/ H_2O_2 systems. The maximum absorbance of H_2O_2 occurs at about 220 nm, but in these cases a high concentration of H_2O_2 is needed to generate sufficient hydroxyl radicals because of low-absorption coefficient of H_2O_2 (19.6 $M^{-1}s^{-1}$) (PARSONS, 2004). This is a drawback of this AOP, as molar absorption coefficient of H_2O_2 is relatively weak in the UV region (OTURAN, AARON, 2014). To overcome it, some researchers/vendors use high-intensity, medium-pressure, broadband UV lamps. On the other hand, high concentration of H_2O_2 scavenges the radicals, making the process less effective by parallel reactions illustrated in Equations 8 to 10 (PARSONS, 2004). This has been observed in literature (GOMES, GANDO-FERREIRA, *et al.*, 2018, RIBEIRO, MOREIRA, *et al.*, 2019, SILVA, Larissa L.S., SALES, *et al.*, 2017).

Equation 8

$$HO\cdot + H_2O_2 \rightarrow HO_2\cdot + H_2O$$

Equation 9

$$HO_2\cdot + H_2O_2 \rightarrow HO\cdot + H_2O + O_2$$

Equation 10

$$HO_2\cdot + HO_2\cdot \rightarrow H_2O_2 + O_2$$

Efficiency of UV/ H_2O_2 for contaminant removal depends on the yields of reactive radicals (e.g., $HO^{\cdot}$, $SO4^{\cdot-}$, and $Cl^{\cdot}$), their reactivities with specific contaminants and the chemistry of the solution, which can impact the distribution and transformation of radicals for example by the presence of scavengers (RIBEIRO, MOREIRA, *et al.*, 2019). In the case of micropollutants in water matrices, water chemical conditions and the targeted contaminants should be considered in the design of the AOP. For example, UV/ H_2O_2 is not considered as sensitive to changes in chemical parameters (pH, chloride, and bicarbonate) as others AOP such as UV/chlorine and UV/persulfate, but a minimization of natural organic matter (NOM) prior to UV/ H_2O_2 is still necessary because NOM can considerably decrease UV transmittance and scavenge major radicals (LI, Wei, JAIN, *et al.*, 2016).

UV/H_2O_2 has been combined with membrane technologies for wastewater treatment for example for treatment of the retentate generated (CAI, WU, *et al.*, 2020, JUSTO, GONZÁLEZ, *et al.*, 2013, UMAR, RODDICK, *et al.*, 2013). When considering the operational aspects of this process, the main concepts are electrical energy consumption per order (EE/O), the UV dose (fluence) and the consumption of hydrogen peroxide. EE/O combines light intensity, residence time and percent destruction into a single measurement by giving the number of kilowatt-hours of electricity necessary to reduce concentration of a contaminant in 1m3 by one order of magnitude, thereby helping scale up to afull-scale design with accuracy. The UV dose (fluence) gives the total energy required to reach the efficiency goal, which in turn depends on pollutant initial concentration and required level of removal (PARSONS, 2004).

Pharmaceutical removal

The limited biodegradability and "pseudo persistence" of many micropollutants render conventional biological and chemical treatments ineffective in their removal. Among advanced treatment technologies employed thus far, AOPs present potential for treating a wide range of emerging contaminants efficiently(KANAKARAJU, GLASS, *et al.*, 2018, TAOUFIK, BOUMYA, *et al.*, 2020). UV/ H_2O_2 in particular has been proven recently to be technically and economically feasible in full scale real MWWTP for disinfection purposes, although not for MP at the very short irradiation times that were used for disinfection (around 4s) (RODRÍGUEZ-CHUECA, LASKI, *et al.*, 2018). Therefore for full scale application for micropollutant removal, optimizations studies are still required. Kinetic data are necessary to predict the extension of micropollutant degradation for a specified duration of tratment, thereby assessing UV/H_2O_2 potential for removing micropollutants (JIN, PELDSZUS, *et al.*, 2012).

Parmaceuticals such as bisphenol A, caffeine, carbamazepine, chloramphenicol, diclofenac, ibuprofen, naproxen, metoprolol, primidone, ronidazole, sulfamethoxazole and trimethoprim have been reported to be highly degraded by UV/ H_2O_2, because their rate constants (k) reacting with HO• are as high as 10^9-10^{10} M^{-1} s^{-1} (GUO, WU, *et al.*, 2018). However, HO• in such situations could be scavenged by water matrices, such as carbonate/bicarbonate and dissolved organic matter (DOM) because these compounds are present in mg.L^{-1} levels - unlike micropollutants, which are in trace concentration – so they have an advantage in consuming hydroxyl radicals. In this case, the particularity of micropollutants of ocurring in very low concentrations, added to the low molar absorptivity of H_2O_2 (which must be compensated by high doses of it), make the UV/ H_2O_2 process of considerably high operating cost (GUO, WU, *et al.*, 2018). For this reason, integrated processes that can reduce the volumes of wastewater to be treated by AOP are particularly desired.

Due to the large variability in molecular structure of pharmaceuticals, some substances are very sensitive to both UV and hydroxyl radicals, other are only sensitive towards one of them, and a few are insensitive to both, so degradation constant rates for pharmaceuticals need to be invetsigated (WOLS, HOFMAN-CARIS, *et al.*, 2013).

Photolysis and oxidation rate data can be evaluated using two approaches: fluence-based pseudo-first order reaction and second order rate constant (k_{OH}) through competition kinetics, in which case a target reference compound is used, usually p-chlorobenzoic acid (p-CBA) (BAEZA, KNAPPE, 2011, SHU, BOLTON, *et al.*, 2013). For fluence-based approaches, micropollutant degradation kinetics by direct UV photolysis can be modeled using Equation 11 (SHU, BOLTON, *et al.*, 2013):

Equation 11

$$\frac{-d[MP]}{dt} = k_d[MP]$$

where k_d (min^{-1}) is the time-based pseudo first-order rate constant for the direct photolysis of each MP. Integration of Equation 2.11 leads to k_d being obtained from the slope of a plot of ln([MP0]/[MP]) vs. reaction time (or else UV dose, in which case the constant uni is $mJ.cm^{-2}$). With the addition of H_2O_2, the overall micropollutant degradation rate constant consists of a photolysis part and oxidation part, shown in Equation 12: (SHU, BOLTON, *et al.*, 2013)

Equation 12

$$\frac{-d[MP]}{dt} = k_d[MP] + k_i[MP] = k_t[MP]$$

Where k_i is the pseudo first-order rate constant for H_2O_2 oxidation (for which, the H_2O_2 concentration can be assumed to be in excess and thus, OH radical concentration is assumed to be constant at its steady-state level during the reaction). Integration of Equation 12 also leads to k_t being obtained from the slope of a plot of ln ([MP0]/[P]) vs. reaction time.

In the case of low pharmaceutical concentrations, the logarithm of degradation (ln MP/MP_0) can be regarded as linear with time or fluence, so equation 12 may be used to determine pharmaceuticals constant degradation rates (WOLS, HOFMAN-CARIS, *et al.*, 2013). The low concentration of the compounds is necessary to avoid the interactions of pharmaceuticals among themselves and with their transformation products, and competition for hydroxyl radicals (WOLS, HOFMAN-CARIS, *et al.*, 2013). Besides, the adoption of equation 12 must be in condition of ultrapure water such as miliQ as solvent, to avoid any interactions or matrix effects in the reactions, as adopted by WOLS, HOFMAN-CARIS, *et al.*, 2013. In any other circumstances, complex secondary reactions are created arising from these interactions. In this case, the competition kinetics approach is used(BAEZA, KNAPPE, 2011, GARCÍA EINSCHLAG, CARLOS, *et al.*, 2003, SHU, BOLTON, *et al.*, 2013). Competition kinetics is used to compare the reaction rates of solutes present together in the same solution and, thus, under absolutely identical conditions. For example, when UV radiation is applied to a solution containing two organic substrates (S1 and S2) and H_2O_2, kinetics can be described by rate-limiting reaction steps shown in Equations 13 to 17 (GARCÍA EINSCHLAG, CARLOS, *et al.*, 2003):

Equation 13

$$H_2O_2 + hv \rightarrow HO\cdot\ + OH\cdot$$

Equation 14

$$HO\cdot + H_2O_2 \rightarrow HO_2\cdot\ + H_2O$$

Equation 15

$$HO\cdot + S1 \rightarrow Products\ k_{S1}$$

Equation 16

$$HO\cdot + S2 \rightarrow Products\ k_{S2}$$

Equation 17

$$HO\cdot + IP \rightarrow Products\ k_{IP}$$

Where IP represents the set of intermediate products that consume hydroxyl radicals through secondary reactions.

Due to the complex interactions that occur in the medium in parallel side reactions, conclusions obtained for pharmaceuticals reaction rate in $mg.L^{-1}$ concentrations may be different from those obtained in trace concentrations, as demonstrated by SHU, BOLTON, *et al.*, 2013: for higher initial compound concentrations, the rate constants decrease. This probably arises because at higher initial pharmaceuticals concentrations, higher by-product formation occurs, which provides scavengers for hydroxyl radicals.

It has been demonstrated that several pharmaceuticals including carbamazepine, diclofenac, sulfamethoxazole, paracetamol and estrone follow pseudo-first order kinetics with respect to PhACs concentration in the range of µg.L^{-1} (SARKAR, ALI, *et al.*, 2014, WOLS, HOFMAN-CARIS, *et al.*, 2013), although these experiments were performed in miliQ water only. SARKAR, ALI, *et al.*, 2014 investigated the effects of background organics as measured by TOC on estrone degradation, representing organics by a solution of potassium hydrogen phthalate (KHP) and reported constant degradation rate in UV/H_2O_2 was not significantly affected by introduction of KHP. However, this study is limited to draw conclusions for micropollutants applications as estrone concentration was in mg.L^{-1} and it's a great simplification to represent organics in a solution using just one compound.

LEE, GERRITY, *et al.*, 2016 assessed kinetic degradation of diclofenac, naproxen, carbamazepine, and meprobamate in real wastewaters previously treated by activated sludge and trickling filter, and they too reported the decrease in micropollutant concentrations during UV and UV/ H_2O_2 treatment could be well described by first-order kinetics with respect to the applied UV doses. Degradation constants was calculated as the slope of plots of the logarithmic relative residual micropollutant concentration as a function of the UV dose. Nonetheless, such studies are still limited in literature and the degradation rate constants of many other pharmaceuticals of interest in real matrices remain a knowledge gap, as noted recently by RIBEIRO, MOREIRA, *et al.*, 2019. This impacts the eventual UV/H_2O_2 scale-up for micropollutant removal.

A considerable amount of research has been published relating to the application of AOPs for the removal of pharmaceuticals in water and wastewater considering process aspects. Given the high number of publications available, Table 3 summarizes results of use of AOP only in context similar to that of the Thesis, that is, applying UV/H_2O_2 for the removal of pharmaceuticals from biologically treated municipal wastewaters or retentate of membrane separation processes. Review papers comprising dozens of other published articles of AOP for wastewater treatment and pharmaceuticals removal in general may be found in (IKEHATA, EL-DIN, *et al.*, 2008, KANAKARAJU, GLASS, *et al.*, 2018, OTURAN, AARON, 2014, YANG, ZHOU, *et al.*, 2014).

Table 3: – A review of removal of pharmaceuticals by UV/H_2O_2 applied in RO retentates or in biologically treated wastewater.

Scale	**Matrix**	**Micropollutants analyzed**	**Operating conditions**	**Removals achieved (%)**	**Reference**
Bench	Real RO retentate from a tertiary treatment in a MWWTP	Indometacin, diclofenac, naproxen, propyphenazone, paroxetine, sulfamethazine, sulfamethoxazol, atenolol, codeine, trimethoprim, carbamazepine	H_2O_2 = 0.04-0.72 $mgH_2O_2.mgTOC^{-1}$, reaction time 0-96.9min, low pressure mercury lamp 8W, λ = 254nm.	30-100	(JUSTO, GONZÁLEZ, *et al.*, 2013)
Bench	Real biologically treated wastewater from a MWWTP	Carbamazepine, diclofenac, metoprolol, clarithromycin, benzotriazole, mecoprop	H_2O_2= 25 $mg.L^{-1}$, reaction time 10 and 30min, low pressure amalgam lamp 9W, λ = 254nm.	99-100	(GIANNAKIS, GAMARRA VIVES, *et al.*, 2015)
Bench	Real biologically treated wastewater from a MWWTP employing activated sludge	Estradiol, ethinylestradiol and estriol	H_2O_2 = 4-16$mg.L^{-1}$, UV dose 24.48-122.4 $kJ.m^{-2}$, low pressure lamp 20W, λ = 254nm.	91-100	(SILVA, Larissa L.S., SALES, *et al.*, 2017)
Bench	Real biologically treated wastewater from MWWTP	Diclofenac, naproxen, carbamazepine, meprobamate	H_2O_2 = 10 $mg.L^{-1}$, UV dose 20-2700 $mJ.cm^{-2}$, low	20-100	(LEE, Yunho, GERRITY, *et al.*, 2016)

	employing activated sludge/trickling filters		pressure mercury lamp , λ = 254nm.		
Full	Real biologically treated wastewater from a MWWTP employing activated sludge	Carbamazepine, lidocaine, terbutryn, 1-H benzotriazole, sulfamethoxazole, metoprolol, gabapentin, o-Desmethyltramadol, Tramadol, Norvenlafaxine, Venlafaxine,oxcarbamazepine, mirtazapine, Tris(2-chloroethyl)-phosphate, N,N-diethyl-m-toluamide, Tris(1-chloro-2-propyl)-phosphate, Tris(1,3-dichloro-2-propyl)-phosphate, Triphenylphosphate, Tolytriazole, Isocyclemone E, Traesolide, Galaxolidone, Tonalide, Galaxolide	H_2O_2 = 0.05-0.5mM, reaction time 4-18s, 16 UV-C lamps 330W, λ = 254nm.	2-95	(RODRÍGUEZ-CHUECA, LASKI, *et al.*, 2018)

Pilot	Real biologically treated wastewater from a MWWTP employing activated sludge. The wastewater was also previously treated: by coagulation-flocculation, by O3-H2O2 and biofilters (Uv/H2O2 is the last step of a multi step treatment plant)	BHA, DEHP, diuron, isoproturon, quinoline, NMP, NPYR, norethindrone, terbutryn, estriol, RDX, PFOA, aniline	H_2O_2 = 5 mg.L^{-1}, UV dose 350-500 mJ.cm^{-2}, λ = 254nm.	43	(PIRAS, SANTORO, *et al.*, 2020)
Bench	Real biologically treated wastewater from a MWWTP employing activated sludge	Bisphenol A, 17β-estradiol and 17α-ethinylestradiol	H_2O_2 = 3mg.L^{-1}, reaction time 10-90min, UV-C lamp 6W, λ = 254nm.	100	(CHAVES, GOMES, *et al.*, 2020)
Pilot	Real biologically treated wastewater from a MWWTP employing activated sludge	Estrone, estradiol, ethinylestradiol, mecoprop, atrazine, terbutryn, NDMA, metaldehyde	H_2O_2 = 3 mg.L^{-1}, UV dose 678-739 mJ.cm^{-2}, 12 low pressure amalgam lamps, λ = 254nm.	45-99	(JAMES, GERMAIN, *et al.*, 2014)
Pilot	Real RO retentate from a tertiary treatment in a MWWTP	Estrone, estradiol, ethiylestradiol, mecoprop, atrazine, terbutryn, NDMA, metaldehyde	H_2O_2 = 16 mg.L^{-1}, UV dose 1775-2026mJ.cm^{-2}, 12 low pressure amalgam lamps, λ = 254nm.	98-99	(JAMES, GERMAIN, *et al.*, 2014)

Bench	Real RO retentate from a tertiary treatment in a MWWTP	Iohexol, lamotrigine, bezafibrate, venlafaxine, sulfamethoxazole, carbamazepine, diclofenac	H_2O_2 = 60 mg.L^{-1}, UV dose 1730-3460mJ.cm^{-2}, medium pressure polychromatic UV lamp, λ = 220-350nm.	20-95	(KAPLAN, MAMANE, *et al.*, 2020)

2.3 Materials and Methods

2.3.1 Reagents and materials

For PhACs analysis by HPLC, CBZ was purchased from US Pharmacopeial Convention (U.S.P., Rockville, MD, USA) as certified reference standard. ACT, DIF, EE2 and SMX chemical reference substances were obtained from Brazilian Pharmacopeial Convention (Rio de Janeiro, RJ, Brazil). Individual stock solutions of 1 $mg.mL^{-1}$ were prepared by dissolving 10±0.02 mg (corrected for purity and water contents) of each standard in 10±0.02 mL of methanol and were stored at -20ºC. All intermediate and working mixed solutions were prepared freshly in methanol by dilution of stock solutions to obtain the required concentrations.

Pre-concentration of the samples, prior to HPLC analysis, was performed by solid phase extraction (SPE) using Strata X cartridges (500 mg, 6 mL polypropylene; Phenomenex®). Samples were filtered (qualitative filter paper, 0.45 µm Polyetherimide (PEI) membrane and 0.22 µm Polyvinylidene Fluoride (PVDF) filter prior to SPE extraction.

For synthetic wastewater preparation, the following aqueous commercial drugs were acquired: Bactrim®, containing SMX, from manufacturer Roche; Still®, containing sodium diclofenac, from manufacturer Allergan; generic drug Carbamazepine, contanining this compound, from manufacturer União Química; and generic drug Paracetamol, contanining ACT, from manufacturer Cimed. EE2 was acquired as high-purity (>98%) powder from manufacturer Sigma-Aldrich Brazil.

Acetonitrile, acetone and methanol used for HPLC and ethanol used for wastewater preparation (to dissolve EE2) were purchased from Sigma-Aldrich Brazil.

2.3.2 Synthetic feed wastewater

A synthetic influent was prepared to simulate wastewater to feed the bench scale AS system. The choice of using synthetic wastewater was made to allow reproducibility of the feed composition, therefore ensuring any observed response can be attributed exclusively to the addition of the PhACs, as this was the only variation of composition introduced in the system throughout the entire period of evaluation.

Composition of synthetic feed was based on RODGERS, HEALY, *et al.*, 2005: D-glucose (610 mg.L^{-1}), meat extract (475 mg.L^{-1}), sodium chloride, calcium chloride, magnesium sulfate (15 mg.L^{-1}), sodium bicarbonate (600 mg.L^{-1}), ammonium chloride (60 mg.L^{-1}) and monosodium dihydrogen phosphate (40 mg.L^{-1}), simulating a high strength domestic wastewater. Its characterization is given in Table 4.

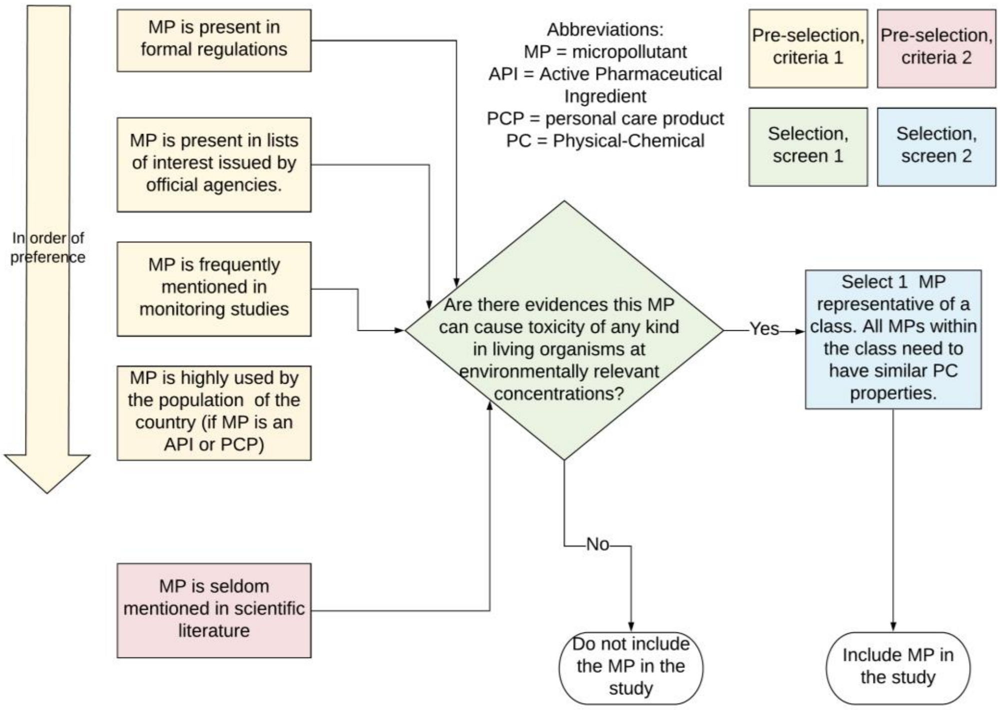
Table 4: Characterization of wastewater considered in this Thesis.

Physical-chemical parameter	**Synthetic wastewater**	**Real Wastewater in WWTP***	**Treated wastewater (bench scale)**	**Treated wastewater (WWTP)****
BOD_5 ($mgO_2.L^{-1}$)	500	161 ± 83	10 ± 15	35
COD ($mgO_2.L^{-1}$)	850 ± 100	216 ± 103	55 ± 24	55
pH	7.0 ± 0.5	7.5 ± 0.3	7.0 ± 0.5	7.0
True color (Pt-Co)	7.0 ± 1.0	Not measured	12 ± 2	6.0
Turbidity (NTU)	7.32 ± 0.5	54 ± 24	1.4 ± 1	4.24

*Characterization provided by FONSECA, Diego Luiz, 2016
**Collected at the secondary clarifier of an activated sludge WWTP.

As previously noted in section 2.1.3, PhACs are not formally regulated by any country yet, with the exception of Switzerland. Thus, some authors have proposed methodologies for the selection of PhACs in wastewater treatment and water reuse studies. A selection methodology for PhACs was elaborated as a part of this Thesis to guide selection of PhACs to be included in the feed synthetic wastewater. Figure 3 represents this methodology, which was presented at the 22nd Brazilian Congress of Chemical Engineering.

Figure 3: Representation of the proposed methodology for PhACs selection.



From the criteria outlined in Figure 3, the five PhACs chosen to be included in the feed synthetic wastewater were:

- Diclofenac - is present in Swiss legislation as a PhACs to be removed from treated municipal wastewater before discharge in the environment. It is also one of the most monitored PhACs in municipal wastewaters and surface waters (as shown in Tables 1 and 2), and for which there is well established evidence of ecotoxic risk at the trace level, even for organisms of higher trophic levels (birds) (Table 5).

- Carbamazepine - like diclofenac, is also present in Swiss legislation and also a PhAC widely monitored in municipal wastewaters and surface waters (as shown in Tables 1 and 2). Its ecotoxic potential is well established (Table 5) and in addition carbamazepine is recognized as very recalcitrant to biological treatment, having already been proposed as an anthropogenic marker(HAI, YANG, *et al.*, 2018), which was confirmed with the results of this Thesis. As a result, it can be considered a reference for future regulatory frameworks, and should therefore be prioritized.

- 17-α-ethinylestradiol – is in the EPA’s Contaminant Candidate List and is recognized as an extremely potent endocrine disruptor in the long-term, with proven effects on sexual characteristics in fish (fathead minnow) even in concentrations of 5 ng.L^{-1} (KIDD, Karen A., BLANCHFIELD, *et al.*, 2007). In addition, it was selected as a “representative” of the class of steroidal hormones, which also includes estrone, estriol and 17-β-estradiol.

- Acetaminophen - a PhAC widely monitored in municipal wastewaters and surface waters (as shown in Tables 1 and 2) and with a well-established ecotoxic potential (Table 5). It was selected as a “representative” of the class of non-steroidal anti-inflammatory drugs, a class that also contains PhACs frequently monitored such as naproxen and ibuprofen. Acetaminophen was prioritized because it has the lowest molecular weight and the smallest molecular dimensions in this class, making it more challenging for membrane retention, which will be addressed in Chapter 3. Furthermore, acetaminophen has recently been identified as one of the five PhACs that most cause chronic toxic effects in aquatic organisms (LINDIM, DE ZWART, *et al.*, 2019). Diclofenac and 17-α-ethinylestradiol have also been identified among these five compounds.

- Sulfamethoxazole - a PhAC widely monitored in municipal wastewaters and surface waters (as shown in Tables 1 and 2) and with well-established ecotoxic potential (Table 5). It was selected as a “representative” of the class of antibiotic drugs.

Considering the five selected PhACs, Table 5 shows some toxic effects caused by them in target organisms when they are in environmentally relevant concentrations (µg.L^{-1}-ng.L^{-1}).

Table 5: A review of ecotoxicological effects caused by the PhACs assessed in this Thesis.

Selected PhAC	**Therapeutic class**	**Toxicity information at trace levels (μg.L^{-1}-ng.L^{-1})**	**Reference**
Diclofenac	Anti-inflammatory	In a mixture with other PhACs, affected: various reproduction aspects and mobility of *D.magma* (crustacean) in multigeneration experiments; body size and reproduction of *H.azteca* (crustacean); various sexual and reproduction functions in *P.promelas* (fish); mobility of *C.dubia* (crustacean); survival and reproduction of *Danio rerio* (fish); growth in *L.minor* (plant) and *P.subcapitata* (algae). Directly correlated with reinal failure in vulture, a bird, which led to a decline of more than 90% in volture population in India in less than a decade.	(OAKS, GILBERT, *et al.*, 2004, SANTOS, ARAÚJO, *et al.*, 2010, VASQUEZ, LAMBRIANIDES, *et al.*, 2014)
Carbamazepine	Anti-epileptic	In a mixture with other PhACs, affected: various reproduction aspects and mobility of *D.magma* in multigeneration experiments; morpholofy, proliferation, gene expressions of liver cells as well as various reproduction aspects of *D. rerio*; morphology, feeding behavior, ability to regenerate of *H.attenuate* (cnidarian); growth and protein production of *P.subcapitata*; immunoefificency, gene expression, hemocyte count of *L.stagnalis* (snail); mobility and reproduction of *C.duphia*.	(SANTOS, ARAÚJO, *et al.*, 2010, VASQUEZ, LAMBRIANIDES, *et al.*, 2014)

17-α-ethinylestradiol	Estrogen hormone	Various reproduction effects on *P. promelas*: feminization of males through the production of vitellogenin mRNA and protein, impacts on gonadal development as evidenced by intersex in males and altered oogenesis in females which eventualy led to a near extinction of this species in its habitat (lake). Widely established effects in other fish species as well. Reproduction effects (first and second generation of adults emerged significantly earlier than control) on *C. riparius* (midge). Phenotypic sex ratios (greater proportions developed as phenotypic females or with mixed sex phenotypes than males) for *L. sylvaticus* (wood frog)	(KIDD, K. A., BLANCHFIELD, *et al.*, 2007, TOMPSETT, WISEMAN, *et al.*, 2013, WATTS, PASCOE, *et al.*, 2001)
Acetaminophen	Anti-inflammatory	In a mixture with other PhACs, affected: various reproduction functions of *D.rerio* and *H.azteca*; growth of *M.spicatum* (plant) and *L.gibba* (plant); protein expression profile of *C.fluminea* (mollusca). Alone, affected kidney, gill and liver function and histology of *O. mykiss* (fish) and decreased its swimming speed; exerted oxidative and neurotoxic effects (measured as changes in biomarkers glutathione-S-transferase and cholinesterase activies) in *P. lineatus* (snail).	(ALMEIDA, NUNES, 2019, CHOI, ALSOP, *et al.*, 2018, VASQUEZ, LAMBRIANIDES, *et al.*, 2014)
Sulfamethoxazole	Antibiotic	In a mixture with other PhACs, affected: morphology, mobility and ability to regenerate of *H.attenuate*; morphology, gene expressions,	(SANTOS, ARAÚJO, *et al.*,

		proliferatio, liver histology, vitellogenin production of *D.rerio*; mobility and morphology of *D.magna*; growth and protein production of P.*subcapitata*; luminescence of *V.fischeri* (bacteria); mortality of *B.calycilforus* (rotifer) and *T.platyurus* (crustacean);	2010, VASQUEZ, LAMBRIANIDES, *et al*., 2014)

To add the selected PhACs to the synthetic feed wastewater, two standard solutions were previously prepared. The first standard solution was prepared by mixing the aqueous commercial drugs containing SMX, DIF, ACT and CBZ with tap water and putting this solution in ultrasound for 10 minutes to facilitate the complete dissolution of the drugs. The concentration of each PhAC reported in the drug package insert was considered to calculate the amount to be added of each drug in the standard solution, so that the concentration of each PhAC in this standard solution was 10 $mg.L^{-1}$. The second standard solution was prepared by dissolving EE2 in ethanol, and the concentration of EE2 in this solution was also 10 $mg.L^{-1}$.

Appropriate amounts of each of the standard solutions were then used to prepare a stock solution containing the five PhACs. This stock solution was spiked in synthetic feed wastewater to give a theoretical concentration of each PhAC firstly of 0.1 $\mu g.L^{-1}$ and secondly of 15 $\mu g.L^{-1}$. Real PhAC concentration was measured by High Performance Liquid Chromatography with diode array detection (HPLC-DAD) after SPE procedure.

2.3.3 Domestic wastewater collection

Domestic wastewater treated at a local wastewater treatment plant (WTTP) was collected at the outlet of the settling chamber and used in oxidation experiments. This WWTP employs activated sludge as biological treatment. Characterization for this wastewater is given in Table 4.

2.3.4 Analytical Methods

Physical-chemical sample characterization

5-day, 20°C Biological Oyxgen Demand (BOD_5), COD, turbidity, true color, pH, Oxygen Uptake Rate (OUR), Mixed Liquor Volatile Suspended Solids (MLVSS) and dissolved organic carbon (DOC) were determined in agreement with the standard procedures (APHA, 2012). Effluent UV absorption spectra were measured in a UV-1800 spectophotometer by Shimadzu®. Pollutants' removal efficiency (E) in percentage was calculated by Equation 18 and in log reduction by Equation 19. In both, C_i and C_e

correspond to the concentrations of each pollutant in the influent and treated effluent, respectively.

Equation 18

$$E(\%) = \left(\frac{Ci - Ce}{Ce}\right) \cdot 100$$

Equation 19

$$E(\log) = \log_{10} \frac{Ci}{Ce}$$

PhAC analysis

Quantification was performed by HPLC-DAD after SPE pretreatment. SPE cartridges were conditioned with 5 mL of methanol, followed by 5 mL of ultrapure water and 5 mL of acid water (acidified to pH 2.5 with chloridric acid).

Samples of 1.0 L of biologically treated effluent were collected weekly, filtered on qualitative filter paper and then vacuum filtered on 0.45 µm PEI membrane and 0.22 µm PVDF membrane. The filtered samples were acidified (to pH 2.5 with chloridric acid), 1 mg of EDTA was added and after homogenization they were kept at rest for 15 minutes until extraction. Each sample percolated the cartridge under vacuum with a flow rate of 3 $mL.min^{-1}$. Cartridges were washed with two 3 mL portions of ultrapure water and dried under vacuum (-35 kPa) for 5 minutes. Analytes were eluted with 3 portions of 3 mL of methanol and a portion of 3 mL of acetone. The obtained solution was dried in a flow of nitrogen gas at a maximum temperature of 47 ºC. The dry extract contained in the tube was reconstituted with 1 mL of diluent solution (water and acetonitrile, in a 1:1 ratio), then vortexed, filtered through a 0.22 µm PVDF membrane and transferred to a vial for chromatographic analysis.

Liquid chromatographic separation of analytes was performed on a Nexera-i (LC-2040C 3D Plus, Shimadzu) system, equipped with a quaternary solvent manager, a solvent degasser unit, an autosampler, a thermostated column compartment and a photodiode array detector. The optimum separation was obtained using a Symmetry C18 column (4.6 x 250 mm, 5 µm; Waters). The mobile phase was composed by acetonitrile

(ACN) and water, degassed in an ultrasonic bath before use. Chromatographic conditions were: injection volume of 50 µL, flow rate 1 $mL.min^{-1}$ and column temperature 30 °C. The optimized gradient of mobile phase was made with a ramp, increasing ACN composition from 40 to 90% over for 10 minutes, then returning to initial condition, the total analysis was 17 minutes (counting stabilization time). Table 6 shows the detection parameters of each PhAC.

Table 6: Retention time and detection wavelength of each pharmaceutical analyzed by HPCL-DAD.

Pharmaceutical	**Retention time (min)**	**Wavelength (nm)**
Acetaminophen	3.00	254
Sulfamethoxazol	5.15	280
Carbamazepine	7.00	280
17αEthinylestradiol	10.28	280
Diclofenac	12.74	280

Analytical curves were constructed for each PhAC, each curve containing five points in the range of 0.1 to 10,000 ppb obtained from dilutions of a standard solution containing the five PhACs. The method was considered validated considering recovery, linearity (measured by the correlation coefficient r obtained for the calibration curve with linear adjustment), detection and quantification limits (Table 7) (MONTEIRO, SPISSO, *et al.*, 2016, SILVA, Larissa L.S., SALES, *et al.*, 2017).

Table 7: Validation criteria for the chromatographic method.

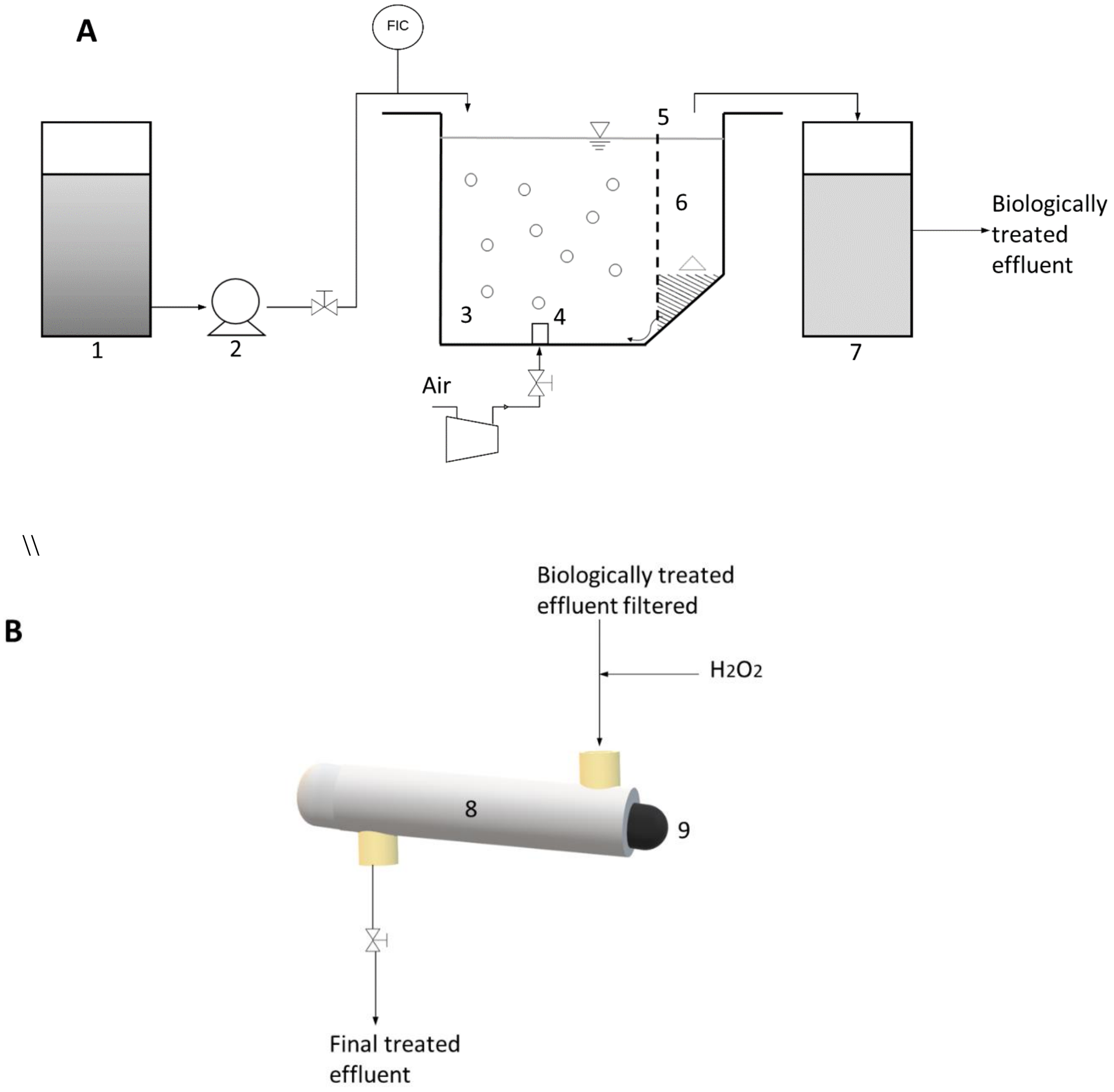
Pharmaceutical	**Recovery (%)**	**Linearity (r)**	**Method Detection Limits (MDL) ($ng.L^{-1}$)**	**Method Quantification Limits (MQL) ($ng.L^{-1}$)**
Acetaminophen	97.7	0.9965	3	10
Sulfamethoxazol	55.8	0.9911	1.5	5
Carbamazepine	109.6	0.9986	1.5	5
17αEthinylestradiol	92.4	0.9999	3	10
Diclofenac	97.2	0.9994	3	10

PhAC removal efficiency was calculated by Equation 18. Whenever the concentration in the treated effluent was below the method quantification limit (MQL), MQL itself was used to calculate the percentage removal.

2.3.5 Experimental set-up and procedure

Experimental setup is illustrated in Figure 4.

Figure 4: Scheme of the experimental set-up, A) continuous and B) batch operation.



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*(1) feed tank, (2) pump, (3) activated sludge aeration chamber (volume 2.2L), (4) air diffuser, (5) adjustable baffle, (6) settling chamber (volume 0.8L), (7) treated effluent tank, (FIC) flow indicator and control, (8) Stainless Steel 316 vessel with working volume of 1.0L. Chamber dimensions: height 145mm, depth 153nm, length 485nm, manufacturer NovaCura, (9) 20 W UV lamp model Germilamp code 10543, 6.8W.m^{-2} fluence with monochromatic emission at 254.0 nm.

Bench scale activated sludge system was continuously operated for a total of 170 days (Figure 4A). Due to the small working volume of the reactor, the daily sludge production is small, therefore, to avoid over-withdrawing of solids, frequent measurements of parameters involving the removal of solids such as Sludge Volume Index (SVI) and Specific Oxygen Uptake Rate (SOUR) were seldom made; turbidity of the treated effluent was measured to indirectly show sludge setteability, instead of SVI, and OUR rather than SOUR was reported. Meanwhile, Mixed Liquor Volatile Suspended Solids (MLVSS) were monitored fortnightly. To control MLVSS growth, sludge purges were make punctually throughout the operation time, whenever necessary to keep MLVSS at 5.0 ± 0.5 g.L^{-1}. Food to Microorganism (F/M) ratio was 0.09 mgO_2.gMLVSS^{-1}.d^{-1}, which is within the recommended range of 0.04-0.1 for systems with prolonged aeration (METCALF, EDDY, 2003). Moreover, considering Long Hydraulic Retention Time (HRT) and Solids Retention Time (SRT) have already been established as optimal conditions for the operation of aerobic bioreactors to maximize the removal of moderately biodegradable micropollutants (HATOUM, POTIER, *et al.*, 2019, LÓPEZ-VELÁZQUEZ, VILLANUEVA-RODRÍGUEZ, *et al.*, 2020, MOWLA, MEHRVAR, *et al.*, 2014), the experimental system was configured as extended aeration, with long aeration time (HRT=48h) and SRT (the reactor was operated with full sludge recirculation). Dissolved oxygen (DO) in aeration tank was kept above 3.0 mg.L^{-1} and pH 7.0 was ± 0.5.

A biocide (sodium azide 100 mg.L^{-1}) was added in treated effluent tank (Figure 4A) to stop microbial activity thereby avoiding overestimation of the results in terms of biodegradation, and sampling for analysis were made from this tank. During acclimatization (i.e. period of time in which changes in the process were observed due to the introduction of PhACS), effluent in this tank was discarded after the after all analyzes have been carried out, but after the acclimatization was finished, it was stored to be used in UV/ H_2O_2 experiments. Once thirty liters of treated effluent were stored, this volume was filtered using 0.45 µm PEI membrane with a vaccum pump (this filtration system has been described previously (MOTTA, BORGES, *et al.*, 2014)), three aliquots (1.0L each) were separated for analysis by HPLC and DOC and the remaining was used in the series of batch UV/H_2O_2 experiments. At the beginning of each experiment, H_2O_2 was added to eflfluent, the vessel was completely filled with it (Figure 4B), the lamp was switched on and counting of UV irradiation time began. At the end of this counting (which corresponds to the reported UV dose), the lamp was manually turned off, the vessel emptied and the effluent was analyzed. In some experiments, H_2O_2 was also added during the experiment using the upper nozzle. AS and UV/H_2O_2 experiments were carried out at 25 ± 2ºC.

2.3.6 Acclimatization of activated sludge biomass

Acclimatization was conducted in the laboratory AS system and consisted of two stages. In the first step, synthetic wastewater without PhACS was added to the aeration chamber. Sludge from a local AS wastewater treatment plant was used as inoculum and mixed with synthetic feed at a 1:3 ratio for startup. Effluent COD was determined in order to check the progress in the acclimatization (LIWARSKA-BIZUKOJC, GALAMON, *et al.*, 2018). Samples were taken from the top of the sludge decanter (represented by the number 6 shown in figure 4A) and analyzed for COD. Once COD removal surpassed 90% and remained in this level, biomass was considered acclimatized to the composition of synthethic influent. Reactor was operated for another twenty days in this condition.

The second acclimatization was necessary as it was found that the introduction of PhAcs affected the AS process. The second stage of acclimatization started when PhACs were added to the influent, in a first stage in a concentration in ng.L^{-1} range and ina s econd stage, in a concentration in ug.L^{-1} range. Samples were collected from the top of the sludge decanter and OUR, COD, true color and turbidity were measured and compared with the reference values obtained in the first step. Bioreactor acclimatization was considered completed in each stage when these parameters were the same than the reference values. After the second stage of acclimatization was completed, the reactor was operated for another 113 days, during which removal of the PhAC was monitored.

2.3.7 Identification of microbial community

Identification of microbial community in the sludge was done using Matrix-Assisted Laser Desorption Ionization-Time-of-Flight Mass Spectrometry (MALDI-TOF MS), this technique has been reported in literature for this application (RAHI, PRAKASH, *et al.*, 2016). Samples of Mixed Liquor (ML) were taken from the reactor on days 20 and 30 (corresponding to the sludge before the insertion of the PhACs) and on days 60 and 146 (corresponding to the sludge after acclimatization was completed). The sample preparation procedure consists of homogenizing ML by vortexing for two minutes, transferring 1 mL of ML to 9 mL of peptonated water and thereafter makes serial dilutions from 10^{-1} to 10^{-7} in peptonated water, homogenizing after each dilution. Aliquots of 100 uL of each dilution were plated on Petri dish contaning Plate Count Agar (PCA), and incubated at 30 °C for 24h. All colonies that were visibly well-isolated on the Petri dishes were then transferred to well plates containing PCA medium. The well plates were incubated at 30 °C for 24h. This second procedure was done to produce enough cells for scraping and transferring colonies to the MALDI-TOF MS plate. Each fresh colony from a well is deposited on the metal plate, in duplicate. A calibration test was performed using a standard consisting of the protein profile of a strain of DH5 alpha *Escherichia coli*. Each colony on the metal plate was subjected to extration in ethanol/formic acid and then crystallized with a matrix (procedure from manufacturer Bruker®). After drying, the plate is inserted into the equipment MALDI Biotyper. The answer for each colony is given in terms of a score between 0-3, where 0-1.7 indicates that there was no safe identification at the genus level. Scores> 1.7 correspond to a likely identification at the genus level. The results were considered valid only when the score> 1.7 and the same result was obtained for the duplicate.

2.3.8 UV/H_2O_2 energy consumption

For energy-consumption comparison purposes, the concept of electrical energy per order of magnitude per m^3 (EE/O) was used. EE/O is defined as the electrical energy (in kWh) required to reduce a pollutant concentration by one order of magnitude (i.e., 90%) in 1.0 m^3 water. For a batch system, EE/O values can be determined from the following Equation 20: (SHU, BOLTON, *et al.*, 2013)

Equation 20

$$EE/O = \left(\frac{P \cdot t \cdot 1000}{V \cdot 60 \cdot \log \frac{Ci}{Ce}} \right)$$

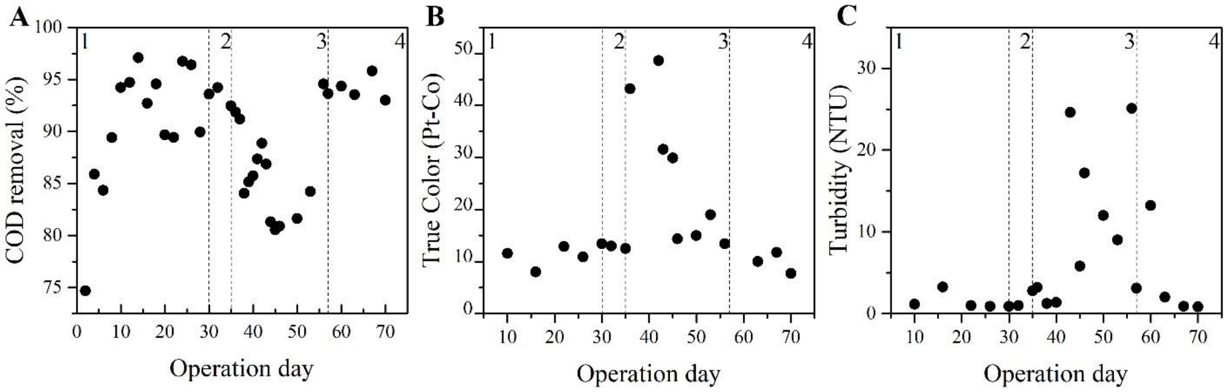
Where P (kW) is the input electrical power to the lamp, t (min) is the irradiation time, V (L) is the volume of water treated and C_i and C_e (M) are the initial and final contaminant (PhAC) concentrations, respectively. EE/O in kWh.m^{-3}.order^{-1}.

2.4. Results

2.4.1 Acclimatizaton of biomass to synthetic influent without PhACs

The performance of AS bioreactor treating synthetic wastewater was evaluated throughout various periods (Figure 5). During the first period, synthetic feed without PhACs was fed to the reactor, to allow biomass acclimatization to the carbon sources of the synthetic feed. Removal of organic matter took ten days to reach the established goal of 90%, and varied between 90-97% in the following 20 days (period 1 in Figure 5). The characterization of the biologically treated effluent obtained in these 20 days was given in Table 4. Biomass OUR value in this period was 311 ± 62 mgO$_2$.L^{-1}d.

Figure 5: A) COD percentage removal B) true color and C) turbidity in the first 70 days of bioreactor operation.



*In all three figures, period 1 corresponds to acclimatization without PhACs addition; period 2: acclimatization with PhACs at range 100 ng.L^{-1} (0.1µg.L^{-1}); period 3: acclimatization with PhACs at range 5-35 µg.L^{-1} and Period 4: acclimatization completed.

2.4.2 Effects of pharmaceuticals addition on the activated sludge process

After completion of acclimatization to the synthetic effluent, a mixture of ACT, SMZ, EE2, CBZ and DIF was added in two stages, the first with a lower concentration range (period 2 in Figure 5) and the second with a higher one (period 3 in Figure 5) in order to assess the effect of the load shock of the mixture on the process. Compared to before PhACs addition, COD removal, turbidity and true color of treated effluent appeared substantially unchanged with lower concentration (0.1 µg.L^{-1}) but changed considerably with higher concentration (ACET 5.8 µg.L^{-1}, SMX 29.4 µg.L^{-1}, DIF 5.6 µg.L^{-1}, CBZ 15.0 µg.L^{-1} and EE2 6.9 µg.L^{-1}). Results indicated that the PhACs effects at this concentration (µg.L^{-1}), which is a concentration range often found in raw municipal wastewater (LUO, Yunlong, GUO, *et al.*, 2014, VERLICCHI, AL AUKIDY, *et al.*, 2012), could influence the treatment efficiency, thus comproving an acclimatization to PhACs was necessary pior to using the sludge as inoculum in the osmotic bioreactor. The results are corroborated by the findings of Liwarska-Bizukjoc et al. 2018 (LIWARSKA-BIZUKOJC, GALAMON, *et al.*, 2018), who reported changes in process parameters when evaluating EE2, DIF and 4-nonylphenol in activated sludge at µg.L^{-1}, and by the findings of AMORIM, MOREIRA, *et al.*, 2016, who evaluated 8 PhACs during 28 days in an aerobic granular sludge-sequencing batch reactor.

Assuming PhACs as chemical stressors, the observed results of increased turbidity can be explained by the response of the microorganisms to this chemical stress: they produce more Extracellular Polymeric Substances (EPS) and Soluble Microbial Products (SMP) to protect themselves from the harsh environment by increasing aggregation (DING, BOURVEN, *et al.*, 2015, NOUHA, KUMAR, *et al.*, 2018, WANG, Zhi Ping, ZHANG, 2010). At high EPS concentrations in the solution, however, flocs are more susceptible to large-scale fragmentation, thus resulting in more smaller-daughter-particles that are more difficult to separate by gravity and are carried more easily (LI, Zhenliang, LU, *et al.*, 2016), resulting in the observed higher turbidity in the biologically treated effluent.

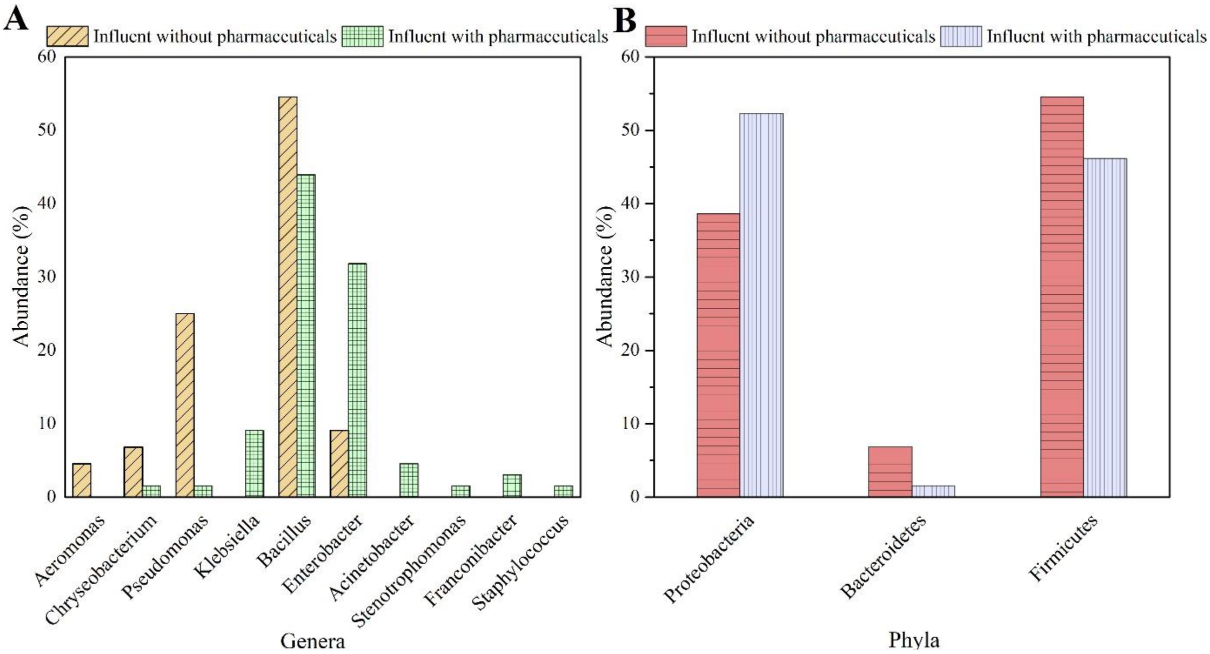
Furthermore, there is a relationship between increased stress in the environment and increased SMP production (WANG, Zhi Ping, ZHANG, 2010). True color is associated primarily with SMP because they represent the largest fraction of soluble organics in aerobic bioreactors fed on simple biodegradable feeds like those in this study (DONG, ZHOU, *et al.*, 2013, GAO, LIU, *et al.*, 2019), thus the stress created by the PhACs introduction can also be linked to the higher color observed in the biologically treated effluent.

COD removal efficiency was also considerably different after PhAC introduction, suggesting an impact on biomass activity corroborated by a decrease of 48% of OUR value in relation to the last measured value before the introduction, falling for the first time below 200 $mgO_2.L^{-1}.d^{-1}$. This immediate effect of drop in oxygen consumption by biomass can be associated with the presence of the PhACs, since this was the only change introduced in the system.

All of these data show that the introduction of shock load of PhACs in $\mu g.L^{-1}$ concentration posed an immediate relavant disturbance on the process, with effects on physical chemical parameters. However, this disturbance was time-dependent: first an acute reduction of biomass activity, followed by some extent of functional recovery during a certain period of time until movement to the original reference. On day 57, OUR, true color, COD and turbidity had values close to the reference values, demonstrating that acclimatization required at least 22 days to complete (period 3 of Figure 5), which was further confirmed by measures in the following days showing the parameters were stable. Therefore quality parameters were only temporarily affected by the load of PhACs, as previously reported (AMORIM, ALVES, *et al.*, 2018).

This behavior suggests that the profile of the microbial community has changed adapt to the presence of these PhACs during acclimatization period. Identification of microorganisms in the mixed liquor carried out before the introduction of the PhACs and once the acclimatization was completed showed that there has been a change in most abundant genera and phyla (Figure 6), which is corroborated by several authors ((AMORIM, ALVES, *et al.*, 2018, HARB, WEI, *et al.*, 2016b, KRUGLOVA, GONZALEZ-MARTINEZ, *et al.*, 2017, PHAN, HAI, *et al.*, 2016)) who have demonstrated that the presence of PhACs in the same concentration range of the present study (low $ug.L^{-1}$) has a clear effect on bacterial communities' relative abundance.

Figure 6: Microorganisms identified in the mixed liquor before the insertion of PhACs and after completing acclimatization to the PhACs.



*Classification by A) genera and B) phyla. Abundance (%) was calculated considering only samples that were identified with score> 1.7 by MALDI-TOF MS, which was the minimum score considered reliable in this work.

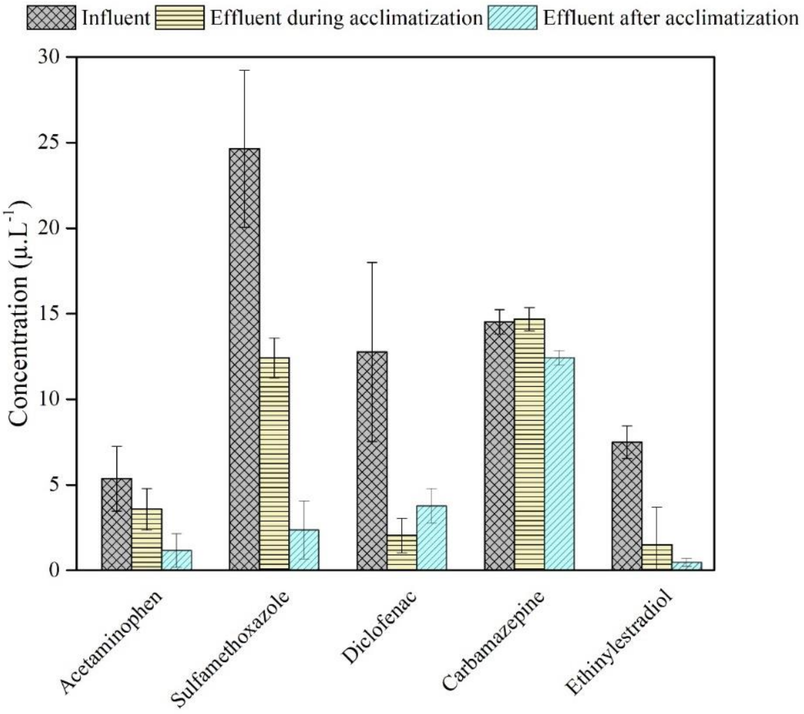
Several genera appeared only after the sludge was exposed to PhACs whereas *Aeromona*s was no longer found, a pattern that was also observed in sludge of a membrane bioreactor after it was fed with 30 micropollutants, including the five analyzed in this study(PHAN, HAI, *et al.*, 2016). Moreover, some genera identified in the ML before the insertion of PhACs were also present after PhACs addition, but in different proportions. In the case of *Pseudomonas*, *Bacillus* and *Enterobacter*, the difference was greater than 10%. Differences in bacterial relative abundance higher than 10% have also been found in aerobic sludge exposed to 10-40 µg.L^{-1} of ACT, SMX, DIF, CBZ and 23 other pharmaceuticals compared to sludge before exposition (HARB, WEI, *et al.*, 2016b). In terms of phylum classification, a decrease in *Firmicutes* in sludge contining PhACs has also been reported by other authors(KRUGLOVA, GONZALEZ-MARTINEZ, *et al.*, 2017, NOVO, ANDRÉ, *et al.*, 2013). Articles on the subject of bacterial diversity and population shifts driven by PhACs use specific analytical methods for analyzing microbial DNA (16s rRNA, polymerase chain reaction) and α- and β-diversity metrics to prove that variations in microbial communities stem from PhACs and not randomness(AMORIM, ALVES, *et al.*, 2018, HARB, WEI, *et al.*, 2016b, KRUGLOVA, GONZALEZ-MARTINEZ, *et al.*, 2017, PHAN, HAI, *et al.*, 2016). The result obtained in this work by MALDI-TOF indicates that the referred works are correct, since a change in the microbial profile was also observed after the introduction of the PhACs.

Effects on biomass, on removal of COD and/or in microbial coomunity profile have already been reported for AS processes during shock loads of PhACs, but until now, only for PhACs concentrations in the range of mg.L^{-1} (OH, CHOI, 2020, VASILIADOU, MOLINA, *et al.*, 2018, ZHANG, Yingying, GENG, *et al.*, 2016, ZHOU, LI, *et al.*, 2019). The results of the present study, however, report that EE2, DIF, SMX, CZ and ACET can cause effects even at much lower concentrations (µg.L^{-1}), though not at ng.L^{-1} level. In other words, PhACs occurring at concentrations usually found in raw municipal wastewater can already affect the process, which implies the need for acclimatization when starting biological reactors for all PhACs concentrations. However, the required acclimatization time is shorter when the input concentration is µg.L^{-1}: it was 22 days for the PhACs in the present study, which is consistent with a similar study for the same concentration level that reported 28 days, though it employed another type of biological reactor and other PhACs. Authors operating AS for PhAC removal at concentration of mg.L^{-1} , on the other hand, employ between 40(ZHANG, Yingying, GENG, *et al.*, 2016) to 60 (OH, CHOI, 2020, ZHOU, LI, *et al.*, 2019) days of acclimatization, hence the importance of specific studies for each case.

2.4.3 PhACs removal

Figure 7 shows measured concentrations of each PhACs on biologically treated effluent during acclimatization (days 35-57) and afterwards (days 57-170).

Figure 7: Concentration of PhACs in the influent and effluent during (days 35-57) and after (days 57-170) acclimatization.

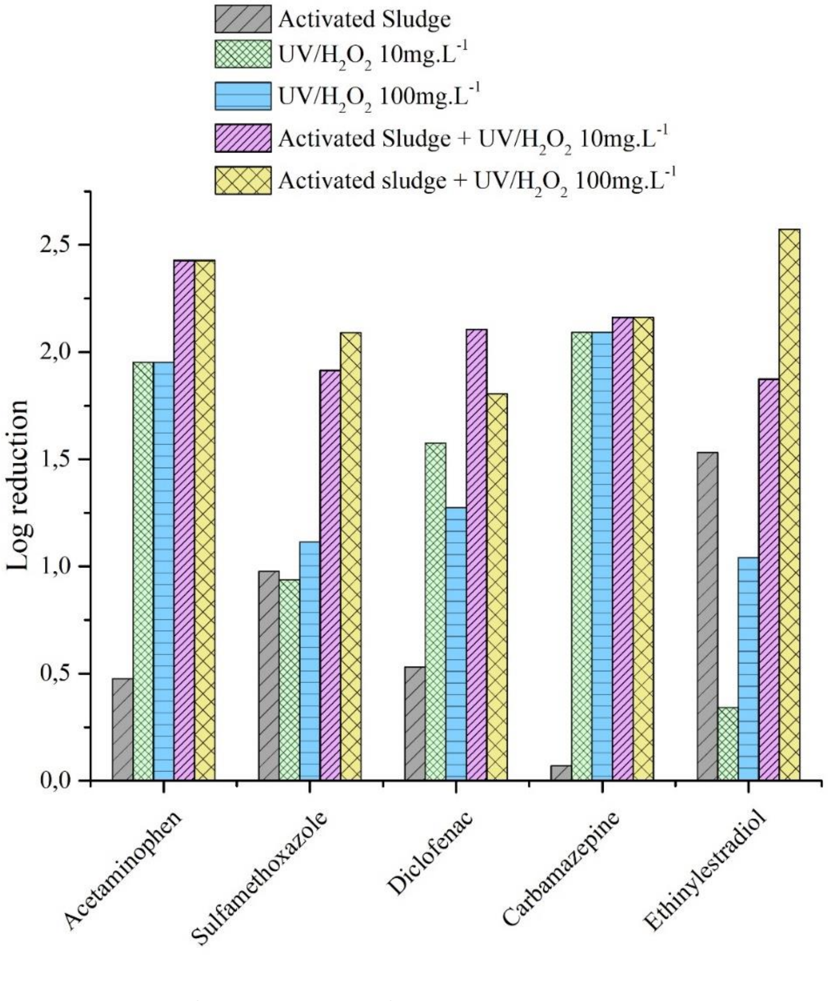


*Error bars represent standard deviations.

Mechanisms of PhACs removal in biological treatment can be divided into abiotic processes (of which the main is sludge sorption) and biotic transformation/degradation processes (RADJENOVIĆ, PETROVIĆ, *et al.*, 2009). Differences in sludge concentrations are known to impact overall sorption capacities, however the relative MLVSS stability maintained at all times of operation likely limited its overall effect on removal rates (HARB, WEI, *et al.*, 2016b). Consequently, the smaller concentration of ACT and SMX in the effluent after acclimatization period was over should be primarily attributed to biomass's increased ability to biodegrade these compounds. Literature results on whether the existence of an acclimatization stage interferes with efficiency of PhACs removal are contradictory (ALIDINA, LI, *et al.*, 2014, BOONNORAT, CHIEMCHAISRI, *et al.*, 2014, FALÅS, WICK, *et al.*, 2016, PHAN, HAI, *et al.*, 2016). The results of the present study indicate that there was a difference for ACT and SMX, but as the sampling period for acclimatization was short, a definitive conclusion could not be reached.

EE2 was the only PhAC to have a high reduction in AS treatment because of its high biodegradability, which has been demonstrated by other authors (CAO, YU, *et al.*, 2008, LÓPEZ-VELÁZQUEZ, VILLANUEVA-RODRÍGUEZ, *et al.*, 2020). Carbamazepine had the lower removal of all MP in biological treatment. The recalcitrance of carbamazepine is well established in the literature, which is why it has been proposed as an anthropogenic marker in the environment (HAI, YANG, *et al.*, 2018). UV/H_2O_2 was used evaluate removal of the residues of PhACs. Figure 8 shows the results in terms of log reduction.

Figure 8: PhAC log reduction in activated sludge only, UV/H_2O_2 only and in the combined process for H_2O_2 doses of 10 and 100 mg.L^{-1} and UV dose 195.84 kJ.m-².



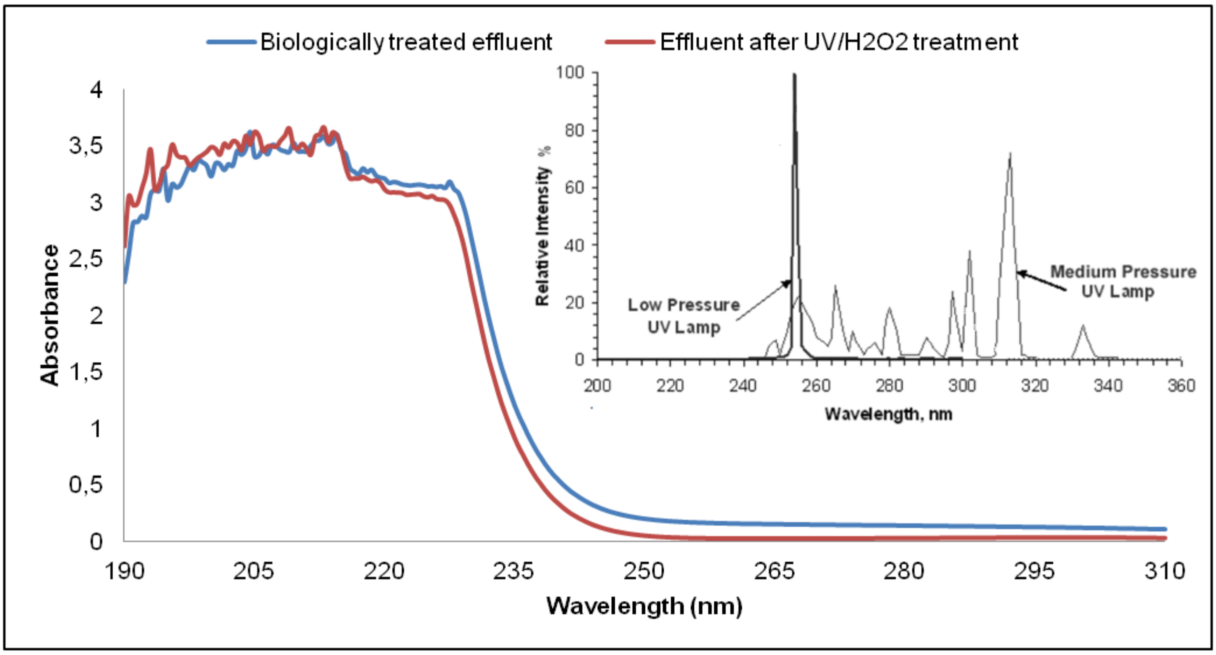
*The reductions informed in this figure were calculated considering the values at the entrance and at the exit of each process, which were: for AS, synthetic feed and biologically treated effluent; for UV/H_2O_2 only, biologically treated effluent before and after UV/H_2O_2; and for AS+UV/H_2O_2, synthetic feed and biologically treated effluent after UV/H_2O_2.

The relative low removal of EE2 with 10 mg.L^{-1} H_2O_2 was attributed to the fact that its concentration was already very low before UV/H_2O_2 (an order of magnitude lower than the others PhACs), therefore the probability of the hydroxyl radical to find this compound in the solution was less than for the other compounds. As a result, the removal only occurred at a relevant level with higher dose of H_2O_2. This did not occur with the other compounds whose concentration in the solution was higher prior to UV/H_2O_2 treatment. However, it is noted that even with a dose of 10 mg.L^{-1} H_2O_2, a high log reduction was achieved for all PhACs when considered the combined process (AS+ UV/H_2O_2). This log reduction translates into a percentage removal above 98% for all PhACs.

2.4.4 Mineralization of biologically treated effluent

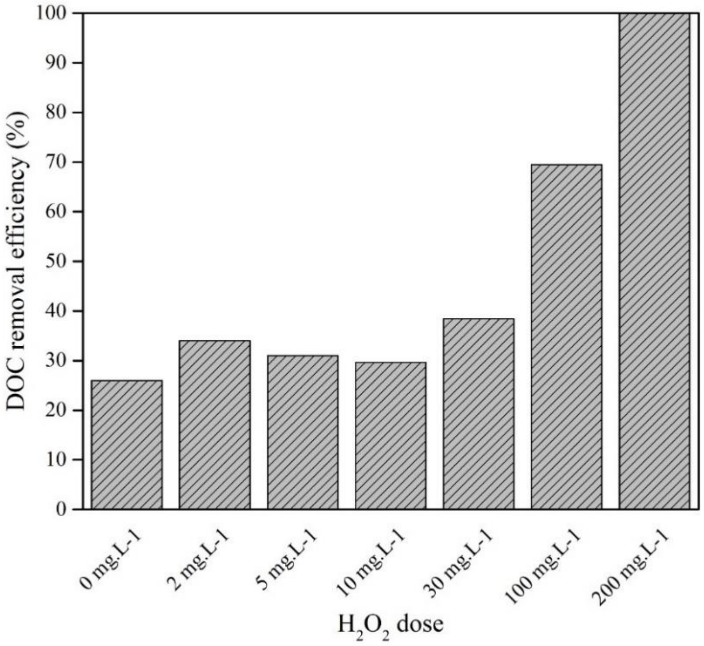
One of the challenges of large scale application of AOPs is the incomplete mineralization of transformation products as indicated by the dissolved organic carbon (DOC) in solution, which has been recognized in several studies (GIANNAKIS, GAMARRA VIVES, *et al.*, 2015, JUSTO, GONZÁLEZ, *et al.*, 2013, RODRÍGUEZ-CHUECA, LASKI, *et al.*, 2018, SARKAR, ALI, *et al.*, 2014, SILVA, Larissa L.S., SALES, *et al.*, 2017). A recent study achieved 65% removal of DOC only after 8.3h of irradiance with low power UV lamp (SARKAR, ALI, *et al.*, 2014). UV absorption spectrum of biologically treated effluents has relevant absorption peaks only below 230 nm, as illustrated in Figure 9.

Figure 9: Absorption spectra in the UV range for biologically treated effluent before and after UV treatment with UV dose 195.84 kJ.m-^{2} and H_2O_2 dose of 10 mg.L^{-1} and emission spectra for low pressure and medium pressure UV lamp.



The absorption peaks are beyond the wavelengths emitted by monochromatic UV light at 254 nm to initiate chemical reaction, as previously reported (SARKAR, ALI, *et al.*, 2014) and corroborated in this Thesis. Therefore, this matrix submitted to UV irradiation with low concentrations of H_2O_2 irradiation hardly changes, and introduction of more H_2O_2 is necessary to form more non-specific hydroxyl radicals, as illustrated in Figure 10.

Figure 10: Percentage removal of DOC from biologically treated effluent by UV/H2O2 with UV dose of 195.84 kJ.m-².



There was an increase in the conversion of organic carbon to CO_2 with H_2O_2 doses starting at 30 mg.L^{-1}. The highest TOC reduction, i.e. total mineralization, was achieved with H_2O_2 dose of 200 mg.L^{-1} , which is equivalent to 22 mgH_2O_2 applied per mg DOC removed. The greater conversion of organics to CO_2 was attributed to the formation of non-specific hydroxyl radicals in sufficient quantities to oxidize a large number of compounds that do not have molar absorptivity at 254 nm. On the other hand, it is known that the increased generation of reactive oxygen species (ROS) can have antagonistic effect, as excessive formation of ROS may act as self-scavengers (GOMES, GANDO-FERREIRA, *et al.*, 2018, RIBEIRO, MOREIRA, *et al.*, 2019, SILVA, Larissa L.S., SALES, *et al.*, 2017). To evaluate this effect, tests were performed with the same dose of UV (195.84 kJ.m^{-2}) and H_2O_2 (30 mg.L^{-1}), with H_2O_2 dosed at once at the beginning of the experiment and in doses equally spaced throughout the duration of UV irradiation; the latter showed results of 10-15% better in the removal of DOC compared to the experiments with single dosage. Thus, subsequent experiments with higher doses of H_2O_2 (30, 100 and 200 mg.L^{-1}) were done with equally spaced H_2O_2 dosing.

DOC reduction appeared to be correlated with H_2O_2 dose and not irradiance time, so new tests were carried out reducing the time of UV irradiance while maintaining the

H_2O_2 dose of 200 mg.L^{-1}. Total mineralization and removal of all PhACs above 98% were also achieved with a lower UV dose, corresponding to 130.56 kJ.m^{-2}. The repetition of this condition in the domestic wastewater collected showed that mineralization also was achieved in this effluent, which had a DOC value of 8 mg.L^{-1}, demonstrating mineralization can also be achieved in a real matrix.

Total mineralization has been identified as the ideal level of organic control, since there is a complete elimination of organics in the solution with a consequent guarantee of eliminating the toxicity from the effluent. (JUSTO, GONZÁLEZ, *et al.*, 2013, SERPONE, ARTEMEV, *et al.*, 2017). However, costs increase dramatically with total mineralization because in addition to the expense with the hydrogen peroxide there is the increase of electricity consumption, as illustrated in the calculation of EE/O considering an UV dose 130.5 kJ.m^{-2}: 54.6 kWh.m^{-3}.order^{-1} for ACT, 95.8 kWh.m^{-3}.order^{-1} for SMX, 102.4 kWh.m^{-3}.order^{-1} for EE2, 51.0 kWh.m^{-3}.order^{-1} for CBZ and 83.0 kWh.m^{-3}.order^{-1} for DIF, whereas studies in the literature usually report EE/O values between 0.4-10.0 kWh.m^{-3}.order^{-1} when they consider the removal only of PhACs in matrices similar to the one used in this study (JAMES, GERMAIN, *et al.*, 2014, SARKAR, ALI, *et al.*, 2014, SHU, BOLTON, *et al.*, 2013).

These results illustrate the trade-off between treatment cost and enhanced DOC removal in UV/H_2O_2 treatment; an alternative would be to seek a lower level of DOC reduction that may already be able to mitigate/minimize the risk of toxicity created by transformation products. Another alternative would be to combine the AOP with membrane-based processes (nanofiltration or reverse osmosis) to reduce the volume to be oxidized, by applying UV/ H_2O_2 only in the retentate generated in such processes.

2.5 Conclusions

In this Chapter, synergistic effects of CBZ, SMX, DIF, EE2 and ACT were evaluated towards activated sludge biomass and quality of biologically treated effluent. In concentrations of 0.1 µg.L^{-1} the PhACs caused no effects; however, their introduction in the range of 10-50 µg.L^{-1} affected the process, as shown by an increase of 3.4 times in true color and 7.7 times in turbidity of biologically treated effluent as well as a decrease in COD removal efficiency and biomass OUR. The results proved the Thesis Hypothesis that PhACs can create effects on AS biomass even at trace concentrations in which they are expected to occur in most raw wastewaters. These effects were however were time-dependent, and after 22 days of continuous operations they all returned to reference values, indicating that this was enough time for a complete acclimatization of the biomass.

Furthermore, the activated sludge process alone was not able to completely remove (i.e. below the detection limit of the method) none of the 5 PhACs considered, even after acclimatization and operating at high SRT and HRT, confirming the Thesis Hypothesis. The removal of each PhACs by this process varied since these PhACs have different biodegradabilities, with carbamazepine being the most recalcitrant of the five, with only 15% biological removal, and EE2, the most biodegradable, with a reduction above 90%. A dose of 10 $mg.L^{-1}$ H_2O_2 and 195.84 $kJ.m^{-2}$ UV reached high log reduction for all PhACs when combined with the AS process, with an overall percentage removal above 98% for all five compounds.

Despite a low dose of H_2O_2 being sufficient for PhAC removal, higher doses of H_2O_2 are mandatory to increase mineralization. The results of this Chapter showed that a high mineralization (70%) of biologically treated effluent can only be achieved with a minimum dose of 100 mg/L of H_2O_2, and complete mineralization, with H_2O_2 dosing of 200 $mg.L^{-1}$ and UV dose of 130.56 $kJ.m^{-2}$. These results were used in the economic analysis in the Chapter 4.

After the end of the operation described in this Chapter (i.e. after 170 days of operation), the biomass (sludge) inside the bioreactor, which was acclimated to PhACs, was collected and then used as an inoculum for the startup of osmotic membrane bioreactor and two controls, as described in Chapter 3, section 3.4. Furthermore, biologically treated effluent was collected and subjected to further treatment as described in Chapter 3, section 3.6.

Chapter 3 - Applicability of osmotic bioreactor using potassium pyrophosphate as draw solution combined with reverse osmosis for removal of pharmaceuticals and production of high quality reuse water

3.1 Introduction and objectives

Rapid population growth, unsustainable water management, increasing environmental pollution and climate change are aggravating the pressure on existing freshwater resources throughout the world . Wastewater treatment is a pragmatic alternative for augmenting fresh water supplies and achieving sustainable development (UNITED NATIONS WATER, 2017) Membrane bioreactor (MBR) has been widely deployed for wastewater treatment and reuse, but it has some operating drawbacks (CARTAGENA, EL KADDOURI, *et al.*, 2013, LUO, Wenhai, PHAN, *et al.*, 2017, SAHAR, DAVID, *et al.*, 2011, WANG, Xinhua, CHANG, *et al.*, 2016). Thus, a new concept of modifying the MBR system to an osmotic membrane bioreactor (OMBR) has been proposed recently as a way to address some of them.

Typical OMBR consists of an activated sludge-based process integrated with a membrane for sludge separation, but using a non-porous forward osmosis (FO) membrane insted of a porous one like in conventonal MBR (WANG, Xinhua, CHANG, *et al.*, 2016). In OMBR, the driving force to permeate water through the FO membrane is the osmostic pressure difference across the membrane, that is created by the use of a draw solution (DS) of high osmotic pressure on one side of the membrane and mixed liquor of small osmotic pressure on the other side. Consequently, DS is diluted by the extraction of water from mixed liquor (LUO, Wenhai, PHAN, *et al.*, 2017, WANG, Xinhua, CHANG, *et al.*, 2016). There is a vast literature about OMBR for wastewater treatment applications (AB HAMID, WANG, *et al.*, 2020, ADNAN, KHAN, *et al.*, 2019, AFTAB, KHAN, *et al.*, 2015, ALTURKI, Abdulhakeem, MCDONALD, *et al.*, 2012a, GURUNG, CHRISTENSEN, *et al.*, 2020, HOLLOWAY, ACHILLI, *et al.*, 2015, LAY, ZHANG, *et al.*, 2012, LUO, Wenhai, HAI, *et al.*, 2015, LUO, Wenhai, PHAN, *et al.*, 2017, LUO, Wenhai, XIE, *et al.*, 2018, LUO, Yunlong, GUO, *et al.*, 2014, NGUYEN, CHEN, *et al.*, 2015, PATHAK, PHUNTSHO, *et al.*, 2020, QIU, TING, 2013, SRINIVASA RAGHAVAN, QIU, *et al.*, 2018, TAN, Jia Ming, QIU, *et al.*, 2015, WANG, Xinhua, CHEN, *et al.*, 2014, ZHANG, Bangxi, SONG, *et al.*, 2017). Their results consistently show considerable water flux decline in the first 20-30 days of operation, attributed both to fouling and to the salinity build-up created inside the reactor that decreases the driving force of the process. Besides, biomass profile changes due to this salinity build-up, with dominant species being taken over by new species with high salinity tolerance (HOLLOWAY, ACHILLI, *et al.*, 2015, QIU, TING, 2013, SRINIVASA RAGHAVAN, QIU, *et al.*, 2018). Inhibition of biomass growth has also been reported (ADNAN, KHAN, *et al.*, 2019, LUO, Wenhai, HAI, *et al.*, 2015, WANG, Xinhua, CHEN, *et al.*, 2014), though biodegradation of organic matter and nutrients (nitrification and denitrification) was not affected even under high salinity conditions (20-50 mS/cm) due to salinity build-up (AB HAMID, WANG, *et al.*, 2020, LUO, Wenhai, PHAN, *et al.*, 2017, PATHAK, PHUNTSHO, *et al.*, 2020, ZHANG, Bangxi, SONG, *et al.*, 2017). High removal of trace organic compounds have also been reported by OMBR (ALTURKI, Abdulhakeem, MCDONALD, *et al.*, 2012a, LUO, Wenhai, PHAN, *et al.*, 2017, LUO, Wenhai, XIE, *et al.*, 2018). The main operational issue raised by these works is the high reverse salt flux (RSF), a key limiting factor in OMBRs (WANG, Xinhua, CHANG, *et al.*, 2016) that occurs because most studies employ a sodium chloride (NaCl) solution as draw solution (DS) (AB HAMID, WANG, *et al.*, 2020, AFTAB, KHAN, *et al.*, 2015, ALTURKI, Abdulhakeem, MCDONALD, *et al.*, 2012a, GURUNG, CHRISTENSEN, *et al.*, 2020, LUO, Wenhai, PHAN, *et al.*, 2017, LUO, Wenhai, XIE, *et al.*, 2018, PATHAK, PHUNTSHO, *et al.*, 2020, TAN, Jia Ming, QIU, *et al.*, 2015, WANG, Xinhua, CHEN, *et al.*, 2014, ZHANG, Bangxi, SONG, *et al.*, 2017). NaCl has a small size that yields a high diffusitivity, which minimizes internal concentration polarization (ICP) on the FO membrane support layer. However, this high diffusivity also leads to the relatively high reverse solute flux (RSF), contributing considerably to the salinity build-up inside the bioreactor, which impacts biomass and increases operating costs for OMBR because of the need of salt replenishment (SHAFFER, WERBER, *et al.*, 2015).

When OMBR is applied for wastewater treatment for the purpose of water reuse it must involve a second step to recover the water, and reverse osmosis (RO) is a possible choice for this aplication. Despite its fundamental role in obtaining reuse water, a limited number of works so far investigated the RO subsequent to OMBR (LUO, Wenhai, HAI, *et al.*, 2016, LUO, Wenhai, PHAN, *et al.*, 2017, ZHANG, Bangxi, SONG, *et al.*, 2017), which constitutes an important gap because, as in any combined process, the second stage of treatment is influenced by the first. For example, the accumulation of solutes in the DS in a closed loop operation becomes a cause for concern when RO is used to continuously recycle the DS to OMBR, as this accumulation may deteriorate the quality of RO permeate in long-term operation. Moreover, some of the biggest advantages of replacing an MBR by an OMBR can only be proved when evalutating the combined OMBR-RO. For example, an important consequence of the high rejection of small dissolved compounds by FO is the reduction of fouling in the subsequent RO membrane (LUO, Wenhai, PHAN, *et al.*, 2017), and the combined process "eliminates" the RO retentate, which is continuously recirculated as DS. Besides, the double barrier FO-RO has the potential to improve the quality of reused water compared to MBR-RO (BLANDIN, LE-CLECH, *et al.*, 2018, LUO, Wenhai, PHAN, *et al.*, 2017, PATHAK, PHUNTSHO, *et al.*, 2020).

Despite these advantages, challenges remain for OMBR-RO implementation (BLANDIN, LE-CLECH, *et al.*, 2018, HOLLOWAY, ACHILLI, *et al.*, 2015, WANG, Xinhua, CHANG, *et al.*, 2016). Some key challenges include the high RSF, whether the quality of the water obtained in the process is superior to that of a comparable processes (MBR-RO) to justify the preferential adoption of the OMBR, what are the effects that arise from the operation of the combined processes and how can they impact the overall operation in the long term. Hence the main aim of this study was to experimentally address these key challenges to provide a general evaluation of OMBR-RO applicability. The objectives of this Chapter were:

- To evaluate OMBR in terms of RSF and biomass biological activity when employing a solution of potassium pyrophosphate ($K_4P_2O_7$) as draw solution (corresponding to parts of the specific objective 3);

- To evaluate the OMBR-RO process in regards to water flux decline in both membranes (FO and RO) (corresponding to parts of the specific objective 3);

- To analyze the diluted DS generated by OMBR for the presence of PhACs, verifying experimentally whether there is accumulation of these solutes in the DS (corresponding to parts of the specific objective 4);

- To evaluate the water quality of RO permeate after the OMBR, comparing it to the obtained by the more conventional MBR-RO process, discussing advantages and shortcomings of the proposed technology (corresponding to specific objective 5)

3.2. Literature Review

3.2.1 Forward osmosis

Forward Osmosis (FO) is a process that utilizes the osmotic pressure gradient between a feed solution (FS) and a draw solution (DS) as the driving force to the water permeation through a semipermeable FO membrane, rather than the external hydraulic pressure like pressure-driven, conventional membrane processes such as MF, UF, NF and RO. Fundamentals for this process are presented below.

Definition

Osmosis is the spontaneous transport of solvent molecules from a dilute solution to a more concentrated solution, called draw solution (DS), across a semipermeable membrane. The driving force is the difference in chemical potential of solvent across the membrane ($\Delta\mu$). At equilibrium, the chemical potential of the pure solvent (μ_a^*) is equal to the chemical potential of the solvent in solution (μ_A) (Equation 21) (ALSVIK, HÄGG, 2013):

Equation 21

$$\mu_A^*(P) = \mu_A(x_A, P + \pi)$$

Where x_A is the mole fraction of the solvent, P is the pressure and π is the osmotic pressure. The water flux through the semi-permeable FO membrane is given by Equation 22:

Equation 22

$$J_w = A\left(\pi_{D,b} - \pi_{F,b}\right)$$

Where J_w is the water flux through the semi-permeable membrane, A is the pure water permeability coefficient of the semi-permeable membrane, $\pi_{D,b}$ and $\pi_{F,b}$ are the bulk osmotic pressures of the draw and feed solutions, respectively. Along with the water flux, there is also a reverse salt flux (RSF) from the DS to the FS. Mathematically, the salt flux from DS to the FS can be estimated by Equation 23 (IBRAR, YADAV, *et al.*, 2020):

Equation 23

$$J_s = B\ (C_{DM} - C_{FM})$$

Where J_s is the RSF, B is the salt permeability (which is solute-dependent), C_{DM} is the concentration of draw solute at the membrane surface, and C_{FM} is the concentration of feed solute at the membrane surface on the feed side. It is important to note that Equations 22 and 23 do not consider the concentration polarization effect in FO, though internal concentration polarization is very important in this process (LUTCHMIAH, VERLIEFDE, *et al.*, 2014). as further discussed in item 2.1.3.

Osmotic pressure of an aqueous solution can be calculated by using the Van't Hoff relation given in Equation 24 (VALLADARES LINARES, LI, *et al.*, 2014):

Equation 24

$$\pi = RT\sum iM$$

Where i is the dimensionless van't Hoff factor for the specific ion, M is the molarity of the specific ion, R is the gas constant (0.08206 $L.atm.mol^{-1}.K^{-1}$), and T is the temperature in Kelvin.

It is important to note that, when taking advantage of spontaneous osmosis, a diluted DS current is obtained. In case this diluted current is the final object of the process, the osmotic process is known as osmotic dilution (SHAFFER, WERBER, *et al.*, 2015). When FO is applied for wastewater treatment and water reuse, however, the end product of the process is the water recovered and, for that, it must involve the reconcentration of the DS, separating it from the permeate of interest. Thus, in this context, FO is not a standalone process, but rather a first step that needs to be followed by a second separation step to recover DS and produce the final water. Reverse osmosis (RO) is the most studied process as the second step for wastewater applications, not only as FO-RO (HOLLOWAY, MILLER-ROBBIE, *et al.*, 2016, VALLADARES LINARES, LI, *et al.*, 2016, VINARDELL, ASTALS, *et al.*, 2020) but also when the FO is coupled to a bioreactor forming an osmotic bioreactor (OMBR), a OMBR-RO (HOLLOWAY, REGNERY, *et al.*, 2014, LUO, Wenhai, PHAN, *et al.*, 2017, ZHANG, Bangxi, SONG, *et al.*, 2017) . Recently, it has been proposed the use of membrane distillation as a second step coupled to FO or OMBR (ADNAN, KHAN, *et al.*, 2019, XIE, NGHIEM, *et al.*, 2013).

Membrane Materials

FO membranes have an asymmetric structure comprised of a dense active layer (AL), that is responsible for membrane selectivity and rejection, and a support porous layer that provides mechanical support (LUTCHMIAH, VERLIEFDE, *et al.*, 2014). Different materials can be used for selective layer in FO membranes. ALSVIK, HÄGG, 2013 can be cited as na example of a review study of most used materials and methods for innovative FO synthesis.

Due to the asymmetric structure of FO membranes, they can be positioned either with the active layer facing the feed side (AL-FS or FO-mode) or the draw solution (AL-DS, also called Pressure-Retarded Osmosis (PRO) (LUTCHMIAH, VERLIEFDE, *et al.*, 2014). It is anticipated that the ideal membrane should possess the following properties: (i) thin selective layer to provide high water permeability and high ion rejection, (ii) a thin porous membrane substrate to lessen internal concentration polarization (ICP), and (iii) low fouling propensity (SHAFFER, WERBER, *et al.*, 2015, TRAN, LIM, *et al.*, 2019).

Over the last decade, researchers and industries have been attempting to develop this ideal membrane. The first membrane developed for commercial scale, which is still the most used for lab-scale experiments with OMBRs, is the asymmetric cellulose triacetate (CTA) flat-sheet membrane with an embedded polyester screen mesh manufactured by the company Hydration Technology Innovations (HTI). With the development of new membrane materials and fabrication technologies, the polyamide thin film composite (TFC) FO membrane has also been commercialized (ZHANG, Bangxi, SONG, *et al.*, 2017). TFC FO membranes are reportedly superior than CTA in terms of higher water permeability, lower salt permeability, better solute rejection and stability at broader pH ranges, and the active layer of the TFC membrane is more hydrophilic, negatively charged and rough than the CTA membrane (DUC VIET, IM, *et al.*, 2020, LUTCHMIAH, VERLIEFDE, *et al.*, 2014, ZHANG, Bangxi, SONG, *et al.*, 2017). MAZLAN, MARCHETTI, *et al.*, 2016 presented a detailed a characterization of comercial CTA and TFC membranes, both provided by the american company HTI, in terms of physical structure, chemical composition, intrinsicic properties, fouling propensity and characteristics of the foulant layer.

Factors affecting mass transport

An ideal FO membrane should have high water flux and low reverse solute transport. The direct relationship between osmotic pressure and water flux is evident from Equations 21 and 22. The factors that most influence water flux (J_w) in FO are the Van't Hoff factor, associated with high osmotic pressure, and diffusivity. However, the phenomenon of concentration polarization can have pronouced flux-limitig effects in FO (CORZO, DE LA TORRE, *et al.*, 2017, IBRAR, YADAV, *et al.*, 2020). In the case of reverse solute transport, it depends on the nature of the solute (LUTCHMIAH, VERLIEFDE, *et al.*, 2014). A clear understanding of the relative contribution of these factors to the final performance is therefore highly relevant in FO process. These factors are further explored below.

Water flux

FO can be accompained by external concentration polarization (ECP) in the same way as RO. ECP happens when the concentration of the solute at the membrane surface differs from that of the bulk solution, but its effects can be largely mitigated by increasing the shear rate and turbulence of flow across the membrane (GRAY, MCCUTCHEON, *et al.*, 2006, IBRAR, YADAV, *et al.*, 2020). Therefore, EPC play an importante role in flux decline in FO only when treating highly saline solutions or when the FO membrane operates at a high water flux (IBRAR, YADAV, *et al.*, 2020). However, Internal Concentration Polarization (ICP) plays a dominant role in flux decline in FO process (IBRAR, YADAV, *et al.*, 2020, SHAFFER, WERBER, *et al.*, 2015, WANG, Xinhua, CHANG, *et al.*, 2016, ZHAO, Shuaifei, ZOU, 2011).

ICP occurs within the support layer of the membrane. When the suport layer faces the DS, the solute can enter and exit this layer via convective water flux and direct diffusion. Since the solute cannot penetrate the dense selective layer of the membrane easily, it will result in a concentration polarization layer within the internal structure of the porous layer, which cannot be reduced by altering the shear rate and/or turbulence of flow. Therefore, ICP is characterized by differing solute concentrations at the transverse boundaries of that layer (ALSVIK, HÄGG, 2013, GRAY, MCCUTCHEON, *et al.*, 2006, TAN, Chien Hsiang, NG, 2008). The result is a reduction in the osmotic pressure gradient across the active layer of the membrane, i.e., a net driving force for the osmostic process smaller than expected by the osmotic pressures in the bulk solutions.

In the orientation with the active layer facing DS, intensity of ICP is not severe since the solutes are not transported by the porous layer (TANG, SHE, *et al.*, 2010). However, in the orientation with the active layer facing the feed, ICP exists not only because solutes must permeate through the support porous layer before they can reach the selective layer, where they are subsequently rejected or diffuse across the membrane, but also because there is a dilution of DS by the water permeating through the active layer (thus ICP in this situation is sometimes referred as dilutive ICP). As a result, ICP is particularly impactant on water flux in this configuration (ALSVIK, HÄGG, 2013, WANG, Xinhua, CHANG, *et al.*, 2016). ICP in both orientations of the FO membrane are illustrated in Figure 11.

Figure 11: Internal concentration polarization in the FO process for an asymmetric FO membrane in orientation a) active layer facing draw solution and b) active layer facing the feed.

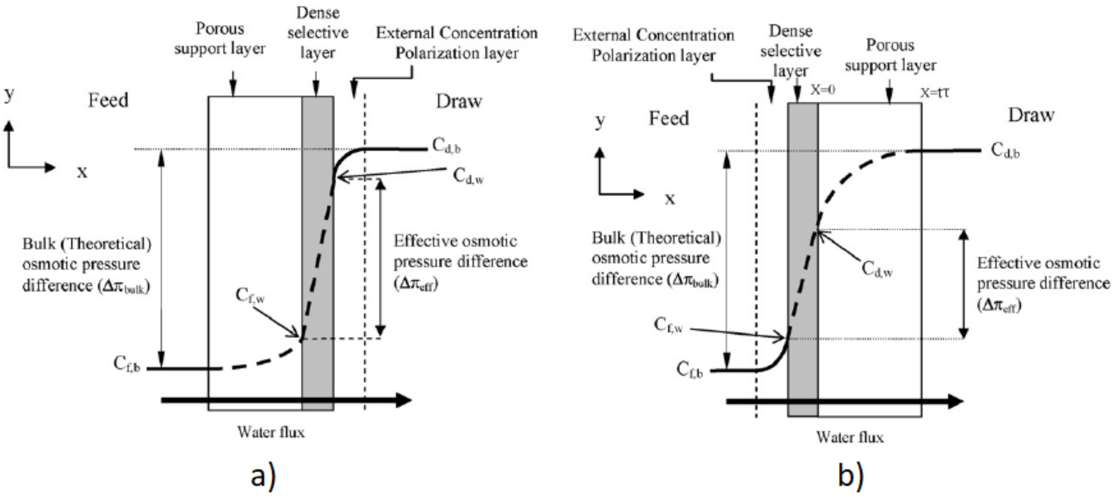


*Figure source: (TAN, Chien Hsiang, NG, 2008)

The solution diffusivity determines the ability of the solute to diffuse in and out of the membrane support layer. Large molecules diffuse more slowly; therefore, dilutive ICP will be more severe with larger molecular weight solutes that cannot diffuse as quickly through the porous support. According to the Stokes-Einstein relation, diffusivity is further influenced by temperature, viscosity of the fluid and particle size. (LUTCHMIAH, VERLIEFDE, *et al.*, 2014). The faster the solute diffuses through the porous layer towards the selective layer, the more it relieves the dilutive ICP effect, thus alleviating ICP. Therefore, there is a direct relationship between solute diffusivity and ICP which, in turn, affect FO water fux. Consequently, a high diffusivity is a highly desired property in DS.

Besides diffusivity, the structural parameter S is another important parameter in FO membranes because it contains information about the characteristics of the support porous layer. S is defined by Equation 25 (ALSVIK, HÄGG, 2013, TANG, SHE, *et al.*, 2010):

Equation 25

$$S = \frac{x\,\tau}{\varphi}$$

Where x is the thickness of the support layer, τ is the tortuosity and φ is the porosity.

S is crucial in FO membrane science because the porous layer also affects mass transport of solutes. Poor mass transfer through these layers not only can be attributed to low diffusivity, as previously mentioned, but also to the thickness and pore size of this layer, represented by S, where large thicknesses and small pores worsen mass transfer. (MANICKAM, MCCUTCHEON, 2017, TAN, NG, 2008). As a result, the degree of internal concentration polarization (ICP) ocurring in FO process, particularly in AL-FS mode when ICP is more pronounced, is partially based on the support layer structural properties that inhibit the diffusive transport, represented by the structural parameter S. This is explained by the theorical model for ICP and FO flux that couples the solution-diffusion theory for the rejection layer and the diffusion convection transport in the support layer (this model is presented in detail by TAN, NG, 2008 and by TANG, SHE, *et al.*, 2010). Such model clearly shows that internal concentration polarization is closely related to the membrane support layer structure, and becomes less severe for membranes with thinner, more porous and minimally tourtous support layers, all of which minimize the diffusion path and enhance back-diffusion of draw solute thus reducing mass transfer resistance. These characteristics are represented by a small value of S (ALSVIK, HÄGG, 2013, SHAFFER, WERBER, *et al.*, 2015).

Consequently, the desired value for S in a FO membrane to minimize ICP is lower than 1500 µm. The comercial FO membrane made of CTA by HTI has a S value between 481-575 µm whereas a comercial RO membrane (BW30, DowFilmtec) has a S of 37500 µm with non-woven support and 14000 µm without it (ALSVIK, HÄGG, 2013). The FO membrane structure is distinctively different from the conventional polyamide TFC structure in conventional RO, where a thick non-woven paper is necessary for mechanical support against high applied hydraulic pressures. The structure in FO is designed to minimize membrane thickness, thus reducing ICP, which is possible considering this membrane is not subject to hydraulic pressure but rather osmotic gradient. It is thus expected the best-perfoming FO membranes will have an ultra-low structural parameter in addition to high selectivity, inert surface chemistry and acceptable water permeance (SHAFFER, WERBER, *et al.*, 2015, TANG, SHE, *et al.*, 2010).

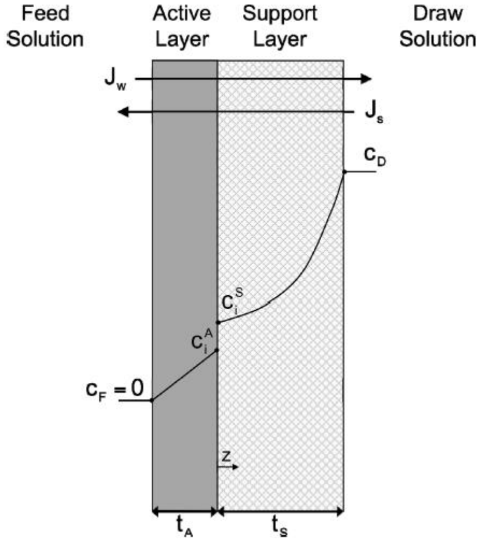
Considering the much less pronounced effect of ICP in the AL-DS orientation, with a consequent greater driving force in the membrane interface, one could expect that the applications of FO membranes for osmotic bioreactors would all be in this orientation; however, this does not occur, and the AL-FS orientation is much more common (HOLLOWAY, ACHILLI, *et al.*, 2015, LAY, CHONG, *et al.*, 2010). This is because it has been widely demonstrated that fouling on the FO membrane is much less intense in the AL-DS orientation (HOLLOWAY, ACHILLI, *et al.*, 2015, LAY, CHONG, *et al.*, 2010, LUTCHMIAH, VERLIEFDE, *et al.*, 2014) because when the membrane porous support is exposed to feed water, foulants can easily enter into the support layer, but are stopped by the dense rejection layer which leads to severe internal clogging in the support structure. Not only there is an immediate effect due to clogging, but clogging also reduces porosity of the support layer, resulting in a greater structural parameter (S). As previously mentioned, ICP has a exponential dependence on S, and the increase in S leads to a drastic increase in ICP that is not offsetted by the absence of dilutive ICP on the porous layer; consequently, there is severe flux decline in AL-DS orientation (TANG, SHE, *et al.*, 2010).

Reverse salt flux

An ideal semipermeable membrane would prevent any dissolved draw solute from permeating into the feed solution. However, no membrane is a perfect barrier, and a small amount of dissolved solute will be transported across the membrane driven by the concentration gradient between DS and FS, a phenomenon known as reverse salt flux (RSF), reverse solute diffusion or salt leakage (PHILLIP, YONG, *et al.*, 2010, WANG, Xinhua, CHANG, *et al.*, 2016).

For the draw solute to transport to the feed solution, it must firstly diffuse through the support layer until it reaches the interface between the support layer and the active layer. Within the support layer, solute diffusion is opposed by the convective flow of solvent and also influenced by its own diffusitivity, as noted in the previous section. Once in the interface between support and active layer, the draw solute partitions into the active layer before diffusing across it. After diffusing across the active layer, the draw solute partitions into the feed solution, which has a negligible concentration of draw solute (PHILLIP, YONG, *et al.*, 2010). This process is illustrated in Figure 12:

Figure 12: Ilustration of the phenomenon of reverse salt flux. C_i^S and C_i^A represent the draw solute concentrations on the support layer side and active layer side, respectively, at the support layer-active layer interface.



*Source: (PHILLIP, YONG, *et al.*, 2010)

Solute leakage decreases the driving force of FO process, i.e., difference of osmotic pressure, because it decreases the osmotic pressure at the draw solution side and increases osmotic pressure in the feed side. To counterbalance this effect, it is required the replenishment of DS, increasing operational costs (WANG, Xinhua, CHANG, *et al.*, 2016). Furthemore, the loss of solute to the feed side may lead to potential damages to this environment, which is of particular relevance in the context of osmotic bioreactors, as they are living systems. Therefore, minimizing RSF is critically important. However, by the description of the transport phenomenon, it is observed that solutes with high diffusivity will more easily penetrate through the porous layer of the membrane and reach the interface where, with the increase of its concentration, they diffuse to the FS because of the concentration gradient. As a result, small, fast-diffusing solutes such as sodium chloride and magnesium clhoride are prone to relatively high reverse solute fluxes (SHAFFER, WERBER, *et al.*, 2015).

In the context of RSF, solutes with high diffusivity are thus a disadvantage, while from the point of view of minimizing ICP, they are advantageous precisely because they reduce the dilutive effect of ICP. As a result of these conflicting effects, when choosing draw solutes, there is a tradeoff between small solute size to limit ICP or large solute size to decrease RSF (SHAFFER, WERBER, *et al.*, 2015). In case the “priority” is to maximize the water flux, the preference should be for small solutes, in order to keep the osmotic pressure gradient across the active layer of the membrane, i.e., the net driving force, relatively high. However if the “priority” is to reduce the RSF, larger solutes whose rejection by the dense FO membrane are preferred.

Draw solution selection

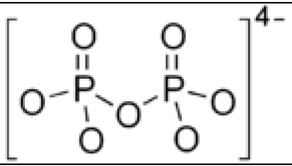
Similar to FO membrane properties, the choice of draw solute can have a large impact on the performance and feasibility of the FO process. The lack of an ideal draw solute is considered a key fator hindering the successful development of the FO (SUWAILEH, JOHNSON, *et al.*, 2019). When choosing an effective draw solute, a number of criteria will need to be satisfied: i) it must be able to generate a high enough osmotic pressure; ii) it must be stable, highly soluble in water and non-toxic; iii) it should have a low viscosity and a high diffusivity to reduce ICP; iv) it should have a molecular size large enough to limit reverse salt flux through the FO membrane active layer, yet small enough to be highly mobile, mitigating ICP; v) it should be available in large amounts at a low cost and finally vi) should be easy to reconcentrate at a competitive cost (JOHNSON, SUWAILEH, *et al.*, 2018, SHAFFER, WERBER, *et al.*, 2015).

Due to these numerous and sometimes conflicting requirements and to the large number of potential solutes that could be used, a number of solutes with very different properties have been tested: fases and volatile compounds, inorganic salts, organic solutes and even nanoparticles (JOHNSON, SUWAILEH, *et al.*, 2018). There is a strong relationship between physico-chemical properties (e.g. diffusivity, ion/molecule size and viscosity) and performance of the draw solute in the active layer and in the supporting porous layer of the membranes. Monovalent salts in general have high diffusitivity because of their small size, thus retarding dilutive ICP, in addition to a low viscotisity. For these reasons they are the most common choice for draw solutes (JOHNSON, SUWAILEH, *et al.*, 2018). NaCl in particular has been the most used salt to make draw solutions, in concentrations between 0.3 and 6 M, often at 0.5 M simulating the osmotic power of seawater (LUTCHMIAH, VERLIEFDE, *et al.*, 2014).

When FO is applied for obtaining water, the selection of the draw solute may also depend on the final use of the water. For instance, if the final use is irrigation, a fertilizer can be used for direct fertigation; this new application, called fertilized-drawn forward osmosis, has been gaining momentum in literature (ADNAN, KHAN, *et al.*, 2019, KIM, Youngjin, LI, *et al.*, 2019, SUWAILEH, JOHNSON, *et al.*, 2019) and refers to the use of the diluted fertilizer used directly to supply water for irrigation, without the need to recover the DS.

Potassium pyrophosphate salt ($K_4P_2O_7$) (CAS Number 7320-34-5), used as draw solute in this Thesis, is a salt that also has properties of fertilizer (CORZO, DE LA TORRE, *et al.*, 2017). It is the first member of the series of polyphosphates, and the most stable of this series, and is known to be biocompatible, non-toxic and highly soluble in water (187g/100mL H_2O at 25°C), where it forms a low viscous solution with pH around 9 (1%v/v)[6]. Characteristics of pyrophosphate anion are given in Table 8.

Table 8: Physical-chemical parameters of pyrophosphate.

Molecular structure	
Formula	$P_2O_7^{4-}$
Molecular weight (g/mol)	173.94

$K_4P_2O_7$ has not yet been tested experimentally in osmotic bioreactors systems and it was chosen as the salt to make the DS for the OMBR in this Thesis. CORZO, DE LA TORRE, *et al.*, 2017 assessed this salt as candidate for draw solute in a FO system, along with potassium formate (HCOOK), magnesium sulphate ($MgSO_4$), sodium polyacrylate, polyethylene glycol and NaCl, and concluded $K_4P_2O_7$ is among the three most promising solutes for use in a pilot scale plant, particularly because of its large molecular size and because it yields high osmotic pressure.

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[6] Informations provided by the manufacturer Sigma Aldrich.

Process characteristics

The use of FO membranes offers potential advantages over current technologies. Some are inherent to nature of the osmotic process e.g. high strength materials are unnecessary due to the lack of high hydraulic pressures (LUTCHMIAH, VERLIEFDE, *et al.*, 2014). Other advantages. related to the process performance, are in different stages of validation in the scientific literature.

An important advantage, already well consolidated in the literature, is the high rejection capacity of FO membranes for trace organic compounds, dissolved solids, pathogens and ions due to the use of the non-porous membrane (LUTCHMIAH, VERLIEFDE, et al., 2014, SHAFFER, WERBER, et al., 2015). This may offer a signifcant advantage in terms of water quality obtained when FO is coupled with a recovery RO step, providing a double membrane barrier, each with high rejection capacity (BLANDIN, LE-CLECH, *et al.*, 2018).

Other advantages traditionally associated with the FO process, such as low fouling propensity and potential of energy savings due to the lack of applied hydraulic pressure, are still debated. Fouling in FO, like in other membrane processes, can be divided into four major types: organic, inorganic (scaling), colloidal fouling and biological, which often happen simultaneously (LI, Lan, LIU, *et al.*, 2017). Fouling causes a decline in water flux and thus can be measured indirectly by measuring water flux over time, while fouling reversibility can be measured by water flux recovery after a physical cleaning. However, in most FO studies, the DS concentration during FO experiments gradually dilutes, so there is a decrease of the osmotic pressure difference. Therefore, flux decline is expected simply because driving force is reduced, which needs to be accounted when assessing fouling in FO. For water flux to be an appropriate fouling indicator, water flux in fouling experiments must be corrected with a baseline water flux under nonfouling conditions (SAUCHELLI TORAN, D'HAESE, *et al.*, 2020).

Lower fouling propensity and high fouling reversiblity compared to pressure-driven membrane processes have been widely associated with FO, especially when wastewater with high fouling propensity is used as feed solution, because the FO process itself does not induce suspended solids and other organic contaminants into the membrane as there is no applied hydraulic pressure (LUTCHMIAH, VERLIEFDE, *et al.*, 2014, VALLADARES LINARES, LI, *et al.*, 2014). The lack of an applied pressure is believed to lead to a looser and less compacted fouling layer, easily removed by simply increasing the cross-flow velocity (SAUCHELLI TORAN, D'HAESE, *et al.*, 2020). Nonetheless, fouling is unavoidable in FO and well documented, as illustrated by the flux decline (%) in relation to the original water flux in Table 9.

Table 9: Summary of recent fouling studies which compare fouling behaviour in membranes in tests performed in FO (AL-FS configuration) and RO mode.

Membrane	Foulant	Operation Mode	Applied Feed Pressure	Draw Solute	Flux Decline (%)	Flux Recovery (%)	Reference
HTI CTA	200 mg.L^{-1} Alginate, 0.5mM Ca^{2+}, 50mM NaCl	FO	-	4M NaCl	55	99	(MI, ELIMELECH, 2010)
		RO	28 bar	-	50	72	
CTA	200 mg.L^{-1} Alginate, 1mM Ca^{2+}, 50mM NaCl	FO	-	5M NaCl	50	87	(LEE, Sangyoup, BOO, *et al.*, 2010)
		RO	31 bar	-	15	0	
HTI CTA	200ppm Silicon Dioxide nanoparticles, 1g.L^{-1} NaCl	FO	-	1.4M NaCl	18	-	(LAY, CHONG, *et al.*, 2010)
		RO	19.2 bar	-	8	-	
HTI CTA	4.2mM Silica, 115mM NaCl, 19m $MgCl_2$	FO	-	4M NaCl	49	98	(MI, ELIMELECH, 2013)
		RO	31 bar	-	51	80	
HTI CTA	100 mg.L^{-1} Alginate, 1 g.L^{-1} Silica, 50mM NaCl	FO	-	5M NaCl	7	95	(KIM, Yeowon, ELIMELECH, *et al.*, 2014)
HTI TFC		FO	-	1.3M NaCl	12	-	

	Synthetic wastewater with EPS	RO	20.7 bar	-	30	-	(KWAN, BAR-ZEEV, *et al.*, 2015)
HTI TFC	200 mg.L^{-1} Alginate, 1mM Ca^{2+}	FO	-	2.5M Glucose	15	99	(XIE, LEE, *et al.*, 2015)
		RO	12.5 bar	-	16	2	
HTI CTA	200 mg.L^{-1} Alginate, 200 mg.L^{-1} Humic acid, 1200 mg.L^{-1} Red Sea Salt and 220 mg.L^{-1} $CaCl_2$	FO	-	70 g.L^{-1} RSS	30	92	(BLANDIN, VERLIEFDE, *et al.*, 2015)
Dow SW30HR and HTI CTA	200 mg.L^{-1} Alginate, 1mM Ca^{2+}, 3.5% NaCl	FO	-	24% NaCl	73	-	(TOW, LIENHARD, 2016)
		RO	50 bar	-	63	-	
Polymeric TFC	500 mg.L^{-1} Alginate, 1000ppm NaCl	FO	-	4M NaCl	65	80	(JANG, Yongsun, CHO, *et al.*, 2016)
		RO	28 bar	1.3M NaCl	0	-	
Polyamide TFC	250 mg.L^{-1} Alginate, 1mM Ca^{2+}, 2 g.L^{-1} NaCl	FO	-	0.6M NaCl	48	96	(LEE, Jinwoo, KOOK, *et al.*, 2017)
SW30HR and HTI CTA	250 mg.L^{-1} Alginate, 1mM Ca^{2+}, 29mM NaCl	FO	-	5M NaCl	52	107	(TOW, LIENHARD V, 2017)
		FO	40 bar	5M NaCl + 40 bar	39	90	

HTI CTA	200 mg.L^{-1} Alginate, 5mM Ca^{2+}, 45mM NaCl	FO	-	1.5M NaCl*	50	92	(SIDDIQUI, SHE, *et al.*, 2018)

*Draw solution concentration was kept constant.

Note: Source of this table: Adapted from Supplementary Materials from SAUCHELLI TORAN, D'HAESE, et al., 2020.

Results from Table 9 show the extent of fouling in FO membranes in terms of flux decline even without applied pressure, but they must be viewed critically since they are studies on a laboratory-scale and employing synthetic foulants, and the hydrodynamic conditions and the chemical composition of fluids in a real process strongly impact the formation of fouling and its reversibility. In addition, comparison between the studies in Table 9 is hampered because different membranes, experimental set-ups, synthetic foulants and feed pressures are employed in each study, and all these factors affect fouling. More importantly, only in the study carried out by SIDDIQUI, SHE, *et al.*, 2018 DS was kept constant, thus correcting flux decline due to decreasing driving force by dilution.

In despite of these considerations, Table 9 illustrates that fouling is relevant in FO operation, challenging the notion that FO is a low fouling process. The extent of fouling depend on the process as is strongly influenced by interplay between membrane surface and interactive foulants in feed solution. Fouling in the FO process is a complex phenomenon which is affected by various physical and chemical aspects including operating modes and hydrodynamics in module, membrane and foulants characteristics, feed water solution chemistry, and draw solution properties (JUNG, RYU, *et al.*, 2020). However, the mechanism of fouling formation may be unique in FO; for example, without hydraulic pressure, the chemical properties between foulants-foulants e.g. molecular weights, hydrophobicity, chemical functional group, and ionic compositions as well as foulant-membrane became the key role of organic fouling in FO (JUNG, RYU, *et al.*, 2020).

Fouling causes a decline in the membrane permeability by forming a cake/gel layer on the membrane surface or blocking the inside membrane pores of the porous support layer (LI, Lan, LIU, *et al.*, 2017). The foulant layer formed on the surface of an FO membrane acts as a barrier, creating a physical resistance, i.e. a cake layer to water permeation. Moreover, this cake later hinders the back diffusion of the salt entering the feed side due to the reverse salt flux, thereby entrapping the salts in the layer. The net result is an elevated osmotic pressure near the membrane surface with consequent decreases in the osmotic difference between feed and draw solutions, causing a water flux decline. This phenomenon is known as cake-enhanced osmotic pressure (DUC VIET, IM, *et al.*, 2020, JUNG, RYU, *et al.*, 2020).

Despite these aspects, fouling in FO membranes does have the interesting characteristic of greater reversibility, usually greater in FO mode than in tests in RO mode while maintaining all the other conditions identical as illustrated in Table 9. This opens the possibility for simpler and cheaper flux recovery processes. The the greater reversibility can be attributed to the lack of applied pressure, and as a result, the previsouly mentioned assumption that FO fouling is looser and less compacted appears to be true to some extent.

Originally, FO was also considered a low energy process. However, it is now established this can only be true in cases of osmotic dilution due to the lack of the step to recover the DS, which is energy-intensive (SHAFFER, WERBER, *et al.*, 2015). For wastewater treatment and reuse applications, however, regardless of the type of process used in the second step, additional energy to recover the original osmotic pressure by concentrating the DS will be required. Thus, the total energy required by the combined system will be likely above that a standalone RO (JOHNSON, SUWAILEH, *et al.*, 2018, SHAFFER, WERBER, *et al.*, 2015). SHAFFER, WERBER, *et al.*, 2015 pointed out that the energy needed to run an FO process with DS regeneration cannot be less than the minimum energy of separation, a minimum which is already close to the operating parameters of recent RO designs. Other potential advantages of FO, such as the aforementioned high rejection capacity or higher fouling reversibility must therefore be considered as motivation for FO in wastewater applications.

3.2.2 Osmotic bioreactor

Definition

Membrane bioreactors (MBR) have been extensively applied for municipal wastewater treatment because, compared with conventional activated sludge technology, they have advantages such as better efluent quality and smaller footprint. In this technology, particle free effluents are produced through the filtration of the activated sludge mixed liquor using microfiltration (MF) or ultrafiltration (UF) membranes, thus allowing a complete sludge retention inside the bioreactor (WANG, Xinhua, CHANG, *et al.*, 2016, ZHANG, Jinsong, LOONG, *et al.*, 2012).

In despite of these advantages, MBR has several drawbacks. Membranes used in MBR are porous, which are not efficient towards rejection of salts and low molecular weight molecules like soluble microbial products (SMP), pesticides or pharmaceuticals, which are of high concern in the context of water reuse. This restricts the reuse possibilities of the MBR permeate (BLANDIN, GAUTIER, *et al.*, 2018, ZHANG, Jinsong, LOONG, *et al.*, 2012). Moreover, the limited retention of these porous MF/UF membranes creates a high fouling potential in subsequent post-treatment with reverse osmosis or nanofiltration membranes (LUO, Wenhai, PHAN, *et al.*, 2017). Apart from this, there is considerable fouling on the MF/UF membranes submerged in the bioreactor, which worsens the process performance by leading to severe flux decline or rapid pressure increase. In the longer term, it requires frequent membrane cleaning, thus directly leading to an increase in operating and maintenance costs (WANG, Xinhua, CHANG, *et al.*, 2016).

Recently, a new concept of modifying the MBR system to an osmotic membrane bioreactor (OMBR) has been proposed as a way to address some of the drawbacks associated to MBR. Typical OMBR can be considered as an extension of a MBR, where the porous membrane (MF or UF) is replaced by a non-porous, osmotically driven membrane, the forward osmosis (FO) membrane (WANG, Xinhua, CHANG, *et al.*, 2016). The vast majority of works with osmotic bioreactors use aerobic conditions, consisting of suspended biomass in the mixed liquor and incorporating the FO system either submerged or as a side-stream module. The concept of a submerged aerobic OMBR replacing a conventional MBR is illustrated in Figure 13.

Figure 13: Concept of submerged OMBR as a modification of an MBR.

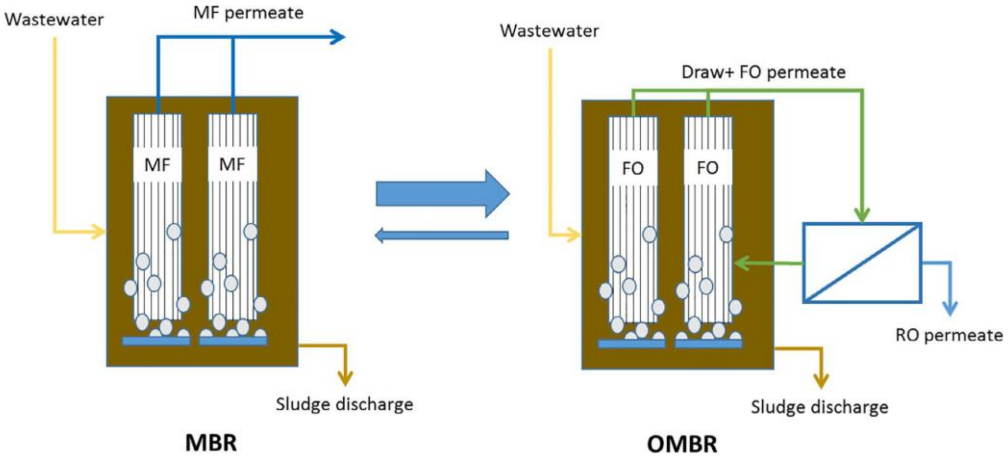

Figure source: (BLANDIN, GAUTIER, *et al.*, 2018).

In the integration of the FO process with conventional activated sludge, FO membranes allow water permeation across the FO membrane from activated sludge feed solution, i.e. the mixed liquor, to the DS. The osmotic pressure difference from one membrane side to the other, due to the low-salinity of activated sludge and the high-salinity of the DS, is the driven force of the OMBR.

Process characteristics

An OMBR applied to wastewater treatment maintains the characteristics of the FO process and therefore has very different characteristics from an MBR. The high retention property of the FO membrane offers the advantage of much higher rejection of particles, macromolecules, ions and even trace organic contaminants such as pharmaceuticals compared to an MBR (HOLLOWAY, ACHILLI, *et al.*, 2015). For example, municipal wastewater contains a wide range of dissolved organic matters and soluble metal salts that can be retained by the FO membrane. This retention constitutes a great advantage of this process, precisely because it maintains solutes that could be foulants in the subsequent stage of RO inside the bioreactor, reducing the fouling in RO, as already demonstrated by (LUO, Wenhai, PHAN, *et al.*, 2017). On the other hand, this retention considerably increases the retention of salts and consequently the conductivity inside the reactor, contributing to the condition known as salinity build-up.

Salinity build-up in OMBR is jointly caused by the FO salt retention capacity and by the reverse salt flux (RSF) and has several implications for the process: i) it leads to a reduced driving force, with economic implications not only because of water flux decline but also because it creates the need for salt replacement periodically; ii) it might contribute to other types of the fouling on the membrane surface, due to inorganic scaling in conjunction with biofouling deposition; and iii) it affects the biomass in terms microbial growth and population profile (AB HAMID, WANG, *et al.*, 2020, HOLLOWAY, ACHILLI, *et al.*, 2015, QIU, TING, 2013, WANG, Xinhua, CHEN, *et al.*, 2014). Since salinity build-up due to rejection of salts by FO is intrinsic to the process, the focus of process optimization is on the aspect that can be mitigated, RSF, which is considered one of the biggest, if not the biggest, obstacle to OMBR implementation (QIU, TING, 2013, SONG, XIE, *et al.*, 2018)

The majority of microorganisms involved in conventional MBR are non-halophilic i.e. do not tolerate higher salinities, as they do not possess the mechanisms to cope with the osmotic stress exerted by an elevated salt environment. Hence, the elevated salinity is likely to impact biological activities, for example, by inhibition of biomass growth (ADNAN, KHAN, *et al.*, 2019, LUO, Wenhai, HAI, *et al.*, 2015, WANG, Xinhua, CHEN, *et al.*, 2014). A significant change on the community profile of activated sludge after the operation of OMBR for 80 days was observed, with almost all the dominant species in the activated sludge taken over by high salt-tolerant new species (QIU, TING, 2013).

Another aspect impacted on the issue of biological activity is the question of the biomass's ability for nitrification and denitrification. Ammonium is present in municipal wastewaters and its continued presence within the OMBR will likely enhance the diffusion through FO membrane to DS, where it can accumulate, eventually deteriorating permeate water quality (PATHAK, PHUNTSHO, *et al.*, 2020). Therefore, nitrification is an important step in OMBR. In the aerobic environment, ammonia-oxidising bacteria (AOB) firstly oxidise ammonium (NH_4) form nitrite (NO_2), followed by nitrite (NO_2) oxidation to nitrate (NO_3) by NOB (AB HAMID, WANG, *et al.*, 2020). Under aerobic conditions, nitrogen remains as nitrate, which, like ammonia, can also accumulate in DS. This has already been experimentally verified by QIU, TING, 2013, thus highlighting the importance of achieving denitrification as well in the OMBR. Denitrifiers bacteria reduce NO_3 to NO_2 and further reduce NO_2 to nitrogen gas (N_2) in anoxic conditions (AB HAMID, WANG, *et al.*, 2020) therefore, for OMBR to achieve satisfactory levels of denitrification, it must operated in oxic and anoxic environments. AOB, NOB and denitrifying bacteria can all be inhibited at high salinites, however, they have different sensivities to increasing salinity (AB HAMID, WANG, *et al.*, 2020). AOB have been consistently reported as less sensitive to increasing salinity; BASSIN, KLEEREBEZEM, *et al.*, 2012 showed que nitritification process can be maintained stable in a sequencing batch reactor until a NaCl concentration of 20 $g.L^{-1}$, though microbial community structure changed; AB HAMID, WANG, *et al.*, 2020, PATHAK, LI, *et al.*, 2018, ZHANG, Bangxi, SONG, *et al.*, 2017 have also demonstrated that there was effective nitrification in OMbr despite of salinity build-up. Denitrification stage was much less explored in the literature, with only two studies found: MORROW, FURTAW, *et al.*, 2018 and QIU, TING, 2013. Both achieved denitrification and simultaneous nitrification in an OMBR with alternating oxic and anoxic phases.

Review of the OMBR literature and knowledge gaps

The characteristics of several OMBR studies for wastewater treatment are shown in Table 10. All the studies presented in Table 10 were developed using activated sludge-type bioreactors, with suspended biomass, under aerobic conditions and coupled with forward osmosis modules, in the same way as in the present Thesis.

Table 10: Characteristics of aerobic osmotic membrane bioreactors applied to wastewater treatment available in the literature.

Membrane area	**Membrane and module type**	**Membrane Material**	**Feed**	**Bioreactor volume**	**Orientation**	**Draw solute**	**Flux decline (%)**	**Total mixed liquor conductivity increase ($mS.cm^{-1}$)**	**Reference**
560 cm²	Submerged plate-and-frame contaning flat-sheets	CTA from HTI	Synthetic	7.56L	Active layer facing feed	NaCl 1M	65.75% in 32 days	50 $mS.cm^{-1}$ in 32 days	(WANG, Xinhua, CHEN, *et al.*, 2014)
360 cm²	Submerged plate-and-frame contaning flat-sheets	CTA from HTI	Synthetic	4.85L	Active layer facing feed	$MgCl_2$ 48.4g.L^{-1} (40bar)	25.64% in 40 days	15 $mS.cm^{-1}$ in 40 days	(SRINIVASA RAGHAVAN, QIU, *et al.*, 2018)
264 cm²	Submerged plate-and-frame contaning flat-sheets	TFC PA from Toray Chemical Korea Inc.	Synthetic	11.5L	Active layer facing feed	NaCl 1.1M	36.79% in 31 days	Did not measure	(PATHAK, PHUNTSHO, *et al.*, 2020)

224 cm^2	Submerged plate-and-frame contaning flat-sheets	CTA from HTI	Synthetic	10L	Membrane support layer facing feed	NaCl 1 M	50.54% in 17 days	20 $mS.cm^{-1}$ in 17 days	(LUO, Wenhai, HAI, *et al.*, 2015)
120 cm^2	Submerged plate-and-frame contaning flat-sheets	Polyamide TFC from Aquaporin Asia (aquaporin proteins embbeded into PA selective layer)	Synthetic	4L	Active layer facing feed	NaCl 0.5 M	34.78% in 20 days	8.7 $mS.cm^{-1}$ in 20 days	(LUO, Wenhai, XIE, *et al.*, 2018)
250 cm^2	Submerged module containing hollow fibers	TFC PA from Singapore Membrane Technology Centre	Synthetic	4L	Tested both	NaCl 0.5 M	45.0% in 5 days	2 $mS.cm^{-1}$ in 5 days	(ZHANG, Jinsong, LOONG, *et al.*, 2012)

360 cm²	Submerged plate-and-frame contaning flat-sheets	CTA from HTI	Synthetic	5.034L	Active layer facing feed	NaCl 49 g.L^{-1} (40 bar)	42% in 64 days	30 mS.cm^{-1} in 64 days	(TAN, Jia Ming, QIU, *et al.*, 2015)
162 cm²	Side stream module containing flat sheets	CTA from HTI	Synthetic	5L	Membrane support layer facing feed	NaCl 6M	83% in 7 days	8 mS.cm^{-1} in 7 days	(ALTURKI, Abdulhakeem, MCDONALD, *et al.*, 2012b)
22.77 cm²	Side stream module containing hollow fibers	TFC from Centre of Technology for Water and Wastewater, University of Technology of Sydney (UTS)	Synthetic	5L	Membrane support layer facing feed	NaCl 30 g.L^{-1}	48.27% in 6.25 days$^{\mathbf{A}}$	Did not measure	(TRAN, LIM, *et al.*, 2019)
Not informed	Submerged plate-and-frame	TFC membrane	Synthetic	Not informed	Not informed	NaCl 10-50 mS/cm	42.85% in 20 days	28 mS.cm^{-1} in 20 days	(GURUNG, CHRISTENSEN, *et al.*, 2020)

	contaning flat-sheets	(manufacturer not informed)							
308 cm²	Submerged plate-and-frame contaning flat-sheets	CTA from HTI	Synthetic	8L	Active layer facing feed	NaCl 35 $g.L^{-1}$	69.33% in 75 days	Did not measure	(AB HAMID, WANG, *et al.*, 2020)
120 cm²	Submerged plate-and-frame contaning flat-sheets	CTA from HTI	Synthetic	4.5L	Active layer facing feed	NaCl 0.5 M	62% in 40 days[B]	32.5 $mS.cm^{-1}$ in 40 days	(AFTAB, KHAN, *et al.*, 2015)Aftab et al. 2015
300 cm²	Submerged plate-and-frame contaning flat-sheets	TFC from HTI	Synthetic	6L	Active layer facing feed	NaCl 0.5M	57.33% in 20 days	7.5 $mS.cm^{-1}$ in 20 days	(LUO, Wenhai, PHAN, *et al.*, 2017)[C]
300 cm²	Submerged plate-and-frame contaning flat-sheets	CTA and TFC from HTI	Synthetic	6L	Active layer facing feed	NaCl 0.5M	CTA: 58.33%, TFC: 66.67% in 30 days	CTA: 15.5 $mS.cm^{-1}$, TFC: 11 $mS.cm^{-1}$ in 30 days	(ZHANG, Bangxi, SONG, *et al.*, 2017)[C]
360 cm²	Side stream module	CTA from HTI	Synthetic	5.03L	Not informed	NaCl 49 $g.L^{-1}$ (40 bar)	35.3% in 100 days	28 $mS.cm^{-1}$ in 100 days	(SRINIVASA RAGHAVAN,

	containing flat sheets								QIU, *et al.*, 2018)
300 cm²	Submerged plate-and-frame contaning flat-sheets	CTA from HTI	Synthetic	6L	Active layer facing feed	NaCl 0.5M, 0.6M NaOAc and 0.3M EDTA-2Na	NaCl: 58.3%; NaOAc: 91.1%; EDTA-2Na: 25.55% in 30 days	NaCl: 16 mS.cm^{-1} NaOAc: 8 mS.cm^{-1} and EDTA-2Na 6 mS.cm^{-1} in 30 days	(LUO, Wenhai, HAI, *et al.*, 2016)[C,D]

[A] with membrane cleaning (physical cleaning, osmotic backwashing and chemical cleaning)
[B] with membrane cleaning (backwashing with NaCl solution as FS and deionized water as DS)
[C] OMBR was coupled with RO for water production
[D] with membrane cleaning (flushing with deionized water)

Some points stand out from the analysis of Table 10. For example, no study so far has carried out tests on a pilot scale, used real wastewaters in the tests or operated the system for periods of time longer than 100 days. Such facts show that, although the OMBR process has been extensively studied in the last decade, its evaluation is still in an initial phase, far from commercial applicability. Therefore, extensive experimental research aimed at its optimization is still required.

Analysis of Table 10 further shows that salinity build-up is high when using NaCl solution as DS, which is illustrated by the high conductivity values of mixed liquor achieved even with short or medium term operation. There are also considerable declines in water flux at the end of operation, partly due to the salinity build-up, that decreases the driving force, and partly due to fouling.

The great prevalence of NaCl solution as DS shows that, despite extensive research on new DS for applications in FO (CORZO, DE LA TORRE, *et al.*, 2017, JOHNSON, SUWAILEH, *et al.*, 2018, LUTCHMIAH, VERLIEFDE, *et al.*, 2014), potential new DS have not yet been incorporated consistently in experimental OMBR tests, being so far restricted to tests with FO systems. This is a gap in the literature that this Thesis aims to fill by using the potassium pyrophosphate salt in the tests.

Finally, it should be emphasized that of the 16 works listed in Table 10, only 3 of them, LUO, HAI, *et al.*, 2016, LUO, PHAN, *al.*, 2017 and ZHANG, Bangxi, SONG, *et al.*, 2017, incorporate the stage of recovery of the DS by RO with production of reuse water. In the 13 other works listed, the diluted DS is reconcentrated through simple salt addition when DS conductivity falls below a setpoint. This constitutes a major knowledge gap, since the reconcentration of the DS is an essential part of the process of treating wastewater and producing reuse water; without it, the final product is a diluted salt stream with no use.

Indeed, the biggest advantages of OMBR-RO process only appear when assessing the processes jointly: for example, the beneficial effect of the high rejection of small dissolved compounds by the FO appears as a reduction of fouling in the subsequent RO. Moreover, it is the double barrier FO-RO that has the potential to improve the quality of reuse water compared to MBR-RO (BLANDIN, LE-CLECH, *et al.*, 2018, LUO, Wenhai, PHAN, *et al.*, 2017, PATHAK, PHUNTSHO, *et al.*, 2020, SAUCHELLI TORAN, D'HAESE, *et al.*, 2020). OMBR can also be seen as an alternative to eliminate the need for continuous disposal of the RO retentate, but only when RO is used to continously recover the DS, recycling it to OMBR. Therefore, an evaluation of the OMBR-RO process for the production of reuse water cannot be complete if it does not evaluate the process in a combined way, and in this Thesis the study of the combined process was emphasizes. The works of LUO, HAI, *et al.*, 2016, LUO, PHAN, *et al.*, 2017 and ZHANG, Bangxi, SONG, *et al.*, 2017, which also assessed the combined process. are presented in detail in item 3.2.4.

Pharmaceuticals removal

Organics transport through non-porous polymeric membranes, which are often used in FO and RO porcesses, is described by the solution-diffusion model. This model involves firstly adsorption of the compounds onto the membrane surfaces, then dissolution into the membrane and subsequently diffusive transport of dissolved molecules through the membrane matrix, which depends on the mobility of the diffusing species (KIM, Sewoon, CHU, *et al.*, 2018). Therefore, the reported rejection of PhACs (and of micropollutants in general) in membrane processes depends on a complex interaction of steric hindrance, electrostatic repulsion, solution effects on the membrane, and solute/membrane properties that can be essentially divided into three broad categories: size exclusion, electrostatic and hydrophobic interactions (BELLONA, DREWES, *et al.*, 2004, NGHIEM, FUJIOKA, 2016).

Size exclusion plays a primary role in the separation of PhACs; the level of rejection of a compounds is determined by the difference between its size and the free-volume (between polymer chains) of the active skin layer of the membrane (NGHIEM, FUJIOKA, 2016). Typically, the rejection of PhACs is correlated to their molecular weight (MW) due to the sieving effect, but despite its wide use, MW is a flawed rejection parameter since it does not provide any information on the PhAC geometry (e.g. length and width), which heavily influences rejection by size. As a result, more recently molecular width (MWd) has been proposed a better paremeter to relate solute size and membrane rejection (NGHIEM, FUJIOKA, 2016).

Size exclusion is a particularly important mechanism when the rejections of neutral compounds are compared, whereas for charged compounds, electrostatic interactions with the membrane have been frequently reported to be a dominant rejection mechanism (BELLONA, DREWES, *et al.*, 2004, NGHIEM, FUJIOKA, 2016). The membrane active layer for most TFC membranes carries a negative charge at usual operating conditions (neutral pH), because they have sulfonic and/or carboxylic acid groups that are deprotonated at neutral pH. Therefore, adsorption of negatively charged foulants present in membrane feedwaters is minimized, increasing the rejection of dissolved salts (BELLONA, DREWES, *et al.*, 2004).

Hydrophobicity is another important parameter as it directly influences the affinities by adsorption on the membrane surface. Hydrophobic compounds adsorb more more easily on the membrane, which is also a hydrophobic material. Hydrophobicity is ypically quantified using the octanol/water partitioning coefficient (Log K_{ow}), and the transition of compounds from hydrophobic to hydrophilic is typically considered to occur at a Log Ko_{w} value of 2 (NGHIEM, FUJIOKA, 2016).

Overall, the rejection mechanisms are similar in FO and in RO membranes. They are governed mostly by size exclusion (or steric interaction) and electrostatic interaction or both (ALTURKI, Abdulhakeem Ali, MCDONALD, *et al.*, 2013, NGHIEM, FUJIOKA, 2016). However, differences in membranes and also in the fundamentals of these processes indicate that differences can be found for several PhACs. For example, the FO membrane is more hydrophilic than the RO membrane (MAZLAN, MARCHETTI, *et al.*, 2016), with obvious impacts on the interactions between hydrophobic and hydrophilic compounds. Futhermorer, reverse salt flux in FO could hinder the pore forward diffusion of the organic solute, leading to a lower adsorption of hydrophobic organic within the membrane and subsequently higher rejection in the FO mode (ALTURKI, Abdulhakeem Ali, MCDONALD, *et al.*, 2013, KIM, Sewoon, CHU, *et al.*, 2018, XIE, NGHIEM, *et al.*, 2012). In addition, it is known that the characteristics of the foulant layer formed on the membrane can influence membrane rejection, and as the fouling profile is different in FO and RO, this may impact on rejection (XIE, NGHIEM, *et al.*, 2012).

For this reason, authors have been studying the rejection of trace organic compounds includig PhACs separately by FO process (ALTURKI, Abdulhakeem Ali, MCDONALD, *et al.*, 2013, JANG, Duksoo, JEONG, *et al.*, 2018, XIE, NGHIEM, *et al.*, 2012). The rejection of PhACs by OMBR, however, is of more interest to this Thesis, therefore a compilation of such studies is presented in Table 11.

Table 11: Literature review of PhACs removal by aerobic OMBR.

Pharmaceuticals analyzed	**Operating conditions**	**FO membrane**	**Overall removal achieved (%)***	**Reference**
Atenolol, atrazine and caffeine	Synthetic wastewater and three draw solutes tested at 0.75M: NaCl, KCl and NaOAc	CTA from HTI	NaOAc: 100%; NaCl: 90-100%; KCl: 95-100%	(PATHAK, LI, *et al.*, 2018) **
Sulfathiazole, sulfamethazine, trimethoprim, norfloxacin, ciprofloxacin, lomefloxacin, enrofloxacin, ofloxacin, tetracycline, oxytetracycline, chlortetracycline, roxithromycin	Synthetic wastewater, draw solution: NaCl solution with 49 g.L^{-1} of salt	CTA from HTI	75-100%	(SRINIVASA RAGHAVAN, QIU, *et al.*, 2018)
Carbamazepine	Synthetic wastewater, draw solution: NaCl solution with NaCl 1 M	CTA from HTI	78-85%	(YAO, DUAN, *et al.*, 2020)
Bisphenol A	Synthetic wastewater, draw solution: NaCl solution at various	CTA from HTI	70-72%	(ZHU, LI, 2013)

	concentrations (to keep water flux constant)			
Ibuprofen, naproxen, sulfamethoxazole, diclofenac, acetaminophen, caffeine, acesulfame, TCEP, TCPP, sucralose, TDCP, DEET, bispheno A, triclocarban, diphenhydramine, atenolol, trimethoprim, fluoxetine.	Real domestic wastewater, draw solution: NaCl solution with 42 $g.L^{-1}$ of salt	CTA from HTI	28-100%	(HOLLOWAY, REGNERY, *et al.*, 2014) 2014**
Clofibric acid, salicylic acid, ketoprofen, fenoprop, naproxen, metronidazole, ibuprofen, primidone, diclofenac, gemfibrozil, propoxur, enterolactone, carbamazepine, pentachlorophenol, DEET, estriol, atrazine, ametryn, amitriptyline, benzophenone, 4-ter-butylphenol, oxybenzone, estrone, bisphenol A, 17α-ethinylestradiol, 17βestradiol, triclosan, 17βestradiol-17-acetate, 4-ter-octylphenol, octocrylene	Synthetic wastewater and 0.5 M NaCl	TFC from HTI	85-100%	(LUO, Wenhai, PHAN, *et al.*, 2017)
Carbamazepine, diclofenac, ibuprofen, naproxen	Synthetic wastewater and NaCl 0.5 M	CTA from HTI	96-100%	(LAY, ZHANG, *et al.*, 2012)

Salicylic acid, paracetamol, phenylphenol, propylparaben, DEET, caffeine, simaxinr, ibuprofen, octylphenol, atrazine, primidone, meprobamate, nonylphenol, naproxen, diuron, carbamazepine, linuron, gemfibrozil, dilantin, triamterene, sulfamethoxazole, ketoprofen, pentachlorophenol, atenolol, estrone, 17α-ethinylestradiol, 17βestradiol, 17αestradio, amtriptyline, androstenedione, estriol, testosterone, triclosan, trimethoprim, eiocholanolone, androsterone, diclofenac, diazinon, fluoxatine, triclocarban, clozapine, omeprazole, chlorpyrifos, hydroxyzine, enalapril, risperindone, simvastatin, methotrexate, verapamil, sim-hydroxy acid	Synthetic wastewater and NaCl 6 M	CTA from HTI	25-100%	(ALTURKI, Abdulhakeem, MCDONALD, *et al.*, 2012b)
Clofibric acid, salicylic acid, ketoprofen, fenoprop, naproxen, metronidazole, ibuprofen, primidone, diclofenac, gemfibrozil, propoxur, enterolactone, carbamazepine, pentachlorophenol, DEET, estriol, atrazine,	Synthetic wastewater and 0.5 M NaCl	CTA from HTI	60-100%	(ZHANG, Bangxi, SONG, *et al.*, 2017)

ametryn, amitriptyline, benzophenone, 4-ter-butylphenol, oxybenzone, estrone, bisphenol A, 17α-ethinylestradiol, 17βestradiol, triclosan, 17βestradiol-17-acetate, 4-ter-octylphenol, octocrylene				
Clofibric acid, salicylic acid, ketoprofen, fenoprop, naproxen, metronidazole, ibuprofen, primidone, diclofenac, gemfibrozil, propoxur, enterolactone, carbamazepine, pentachlorophenol, DEET, estriol, atrazine, ametryn, amitriptyline, benzophenone, 4-ter-butylphenol, oxybenzone, estrone, bisphenol A, 17α-ethinylestradiol, 17βestradiol, triclosan, 17βestradiol-17-acetate, 4-ter-octylphenol, octocrylene	Synthetic wastewater and 0.5 M NaCl	Polyamide TFC from Aquaporin Asia (aquaporin proteins embbeded into PA selective layer)	78-100%	(LUO, Wenhai, XIE, *et al.*, 2018)

*PhAc removal by OMBR is the complementary result of biological degradation and FO membrane rejection.

** These studies include a MF inside the OMBR to control salinity build-up. However, they were included because the impact of these different conditions on PhACs removal is expected to be small.

Note 1: Results in this Table consider removal by the OMBR only, i.e., without contribution from the RO stage, when existing.

Note 2: Since the FO permeate sample is diluted with the initial draw solution, the concentration of the compounds was calculated indirectly by mass balance or by direct measurement of the DS, but considering the dilution factor of the original DS.

Note 3: The concentration of PhACs in the feed in the results in this table was in the environmentally relevant range.

The high rejection of pharmaceuticals (PhACs) by FO membrane for most PhACs, demonstrated in Table 11, is one of the major advantages of using OMBRs over conventional MBR (HOLLOWAY, ACHILLI, *et al.*, 2015). The porous membranes of na MBR do not allow satisfatory removals of these compounds. However if OMBR is combined with RO to produce freshwater, PhAcs are to be subject to a double barrier of membranes, thereby opening the possibility of producing water of better quality than in the conventional MBR-RO process, since the initial concentration of PhAcs in the RO feed will already be considerably lower than in the effluent of MBR feeding RO. This was therefore one of the hypotheses to be tested in the present Thesis.

3.2.3 Reverse osmosis

Definition

Reverse Osmosis (RO) is a membrane-based process that requires high hydraulic pressure applied to the semi-permeable membrane, so it can exceed the osmotic pressure of the feed solution, generating two streams: permeate, containing the water depleted of salt as a low-pressure stream, and retentate[7]. Physical-chemical characteristics of retentate depend on the quality of the feed influent, the quality of the produced permeate, recovery rate (may vary from 35% to 85%), the pretreatment method (added chemicals) and cleaning procedures used, but they always contain almost all the contaminants presented in the original feed at much higher levels (CAI, WU, *et al.*, 2020, PÉREZ-GONZÁLEZ, URTIAGA, *et al.*, 2012).

The passage of water and rejection of dissolved matter by RO is commonly predicted with the solution–diffusion model (which neglects transport by convection (BAKER, 2004, WARSINGER, CHAKRABORTY, *et al.*, 2018). The water flux J_w is linked to the pressure and concentration gradients across the membrane by the Equation 26 whereas the salt flux, J_s, across a reverse osmosis membrane is described by Equation 27 (BAKER, 2004).

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[7] Retentate and concentrate in the context of RO are synonyms.

Equation 26

$$J_w = A\,(\Delta p - \Delta\pi)$$

Equation 27

$$J_s = B\,\left(C_f - C_p\right)$$

Where Δp is the applied hydraulic pressure, $\Delta\pi$ is the osmotic pressure differential across the membrane, A is a constant, B is the salt permeability constant and C_f and C_p are the salt concentrations on the feed and permeate sides of the membrane, respectively.

Most commercially available RO membranes Thin-Film Composite (TFC) with active layer made of polyamide, fabricated by forming a dense homonegeous aromatic polyamide barrier layer on a microporous support such as polysulfone or polyethersulfone via an interfacial polymerization process (KANG, CAO, 2012, WARSINGER, CHAKRABORTY, et al., 2018) . Compared with cellulose membrane, the TFC aromatic polyamide membrane exhibits superior water flux and salt rejection, resistance to pressure compaction, wider operating temperature range and pH range, and higher stability to biological attack; therefore, it is the dominating RO material in membrane field nowadays (KANG, CAO, 2012). Solutes and particles in the atomic/ionic range of 1 angstrom to 1 nm are in theory rejected by this membrane by size exclusion (WARSINGER, CHAKRABORTY, *et al.*, 2018). However, removal of target constituents from an aqueous solution by these polymeric RO membranes vary, as they depend on many factors such as physicochemical properties, membrane type, and operational conditions, as previously discussed.

Applications in wastewater treatment

RO has been extensively used in tertiary wastewater treament since it can achieve high removals of constituents like dissolved solids, organic carbon, inorganic ions, and regulated and unregulated organic compounds, and has been show to be one of the most effective treatment process to reduce ecotoxicity and genotoxicity in secondary treatment municipal wastewater (FARIAS, HOWE, *et al.*, 2014, RODRIGUEZ-MOZAZ, RICART, *et al.*, 2015). RO membranes can reduce 98% of biological chemical demand (BOD), 96% chemical oxygen demand (COD), 96% or higher of total organic carbon (TOC) and between 95-99% of endrocrine disruptor compounds and high molecular weight organic constitutents such as humic and fulvic acids. RO generally removes most compounds better than other engineered or natural alternatives (WARSINGER, CHAKRABORTY, *et al.*, 2018).

In addition, RO has the capacity, theorically, to completely remove viruses and other pathogens by size exclusion. However, due to its modular design, a full-scale membrane installation contains a large number of O-ring seals, interconnectors, glue lines joining membrane sheets and other potential locations, where small leaks may occur (PYPE, LAWRENCE, *et al.*, 2016). Consequently, it cannot be assumed that the actual performance of pathogen removal corresponds to the theoretically achievable value without continuously demonstrating the performance, a fact long recognized by regulating authorities ((BLANDIN, LE-CLECH, *et al.*, 2018, HOLLOWAY, MILLER-ROBBIE, *et al.*, 2016, PYPE, LAWRENCE, *et al.*, 2016). As a result, RO systems, in general, are not recognized for pathogen removal by regulating authorities, and additional disinfection method, such as UV irradiance, is employed (HOLLOWAY, MILLER-ROBBIE, *et al.*, 2016), consequently increasing capital and operating expenses.

RO is increasingly becoming a viable technology for wastewater reclamation. Its large-scale implementation as the last physical removal process in the treatment train has been rapidly increasing worldwide, benefited by membrane cost reduction, process improvement and accumulation of operational experience, modular construction and small footproint and, most importantly, efficacy in removing a wide spectrum of pollutants, both conventional and emerging (HOLLOWAY, MILLER-ROBBIE, *et al.*, 2016, PIRAS, SANTORO, *et al.*, 2020, PYPE, LAWRENCE, *et al.*, 2016, ZHAO, Yan, SONG, *et al.*, 2010). As a result, RO is now considered one of the most common processes in treatment trains employed for potable reuse applications, either indirect or direct potable reuse, as well as production of high quality reuse water in general ((HOLLOWAY, MILLER-ROBBIE, *et al.*, 2016, PIRAS, SANTORO, *et al.*, 2020, PYPE, LAWRENCE, *et al.*, 2016, ZHENG, YU, *et al.*, 2018).

Nevertheless, membrane fouling has largely constricted the performance and economics of this process, as it is a prevalent problem in water reclamation aplications due to the nature of feed wastewater (KENT, FARAHBAKHSH, *et al.*, 2011, ZHAO, Yan, SONG, *et al.*, 2010, ZHENG, YU, *et al.*, 2018). The general types of RO fouling are inorganic (scaling), particulate, biological, and organic fouling. Particulates tend to foul the membane surface by covering the surface and blocking pores and plugging the spacer in spiral wounds elements or bundles in hollow fibers elements, and microorganisms, especially bacteria, irreversibly adhere on the membrane surface and multiplicate fast in the presence of feed water nutrient (ALHADIDI, KEMPERMAN, *et al.*, 2011, KENT, FARAHBAKHSH, *et al.*, 2011, ZHENG, YU, *et al.*, 2018).

Pretreatment is employed to alleviate fouling potential, thus reducing the frequency of chemical cleanings in RO membrane, which lowers its lifetime. Key concerns of pretreatment processes to prevent fouling in RO membranes in wastewater treatment are the removal of suspended particulates, colloids, and dissolved compounds, preventing bacterial growth and inhibiting scaling formation (ZHENG, YU, *et al.*, 2018). Though inorganic and particulate fouling can be mitigated to some extent by using appropriate pretreatment (Coagulation, adsorption, cartidge filters, MF, UF, and dosage of antiscalants and bactericides) and by limiting water recovery, biological and organic fouling can be more difficult to control (FARIAS, HOWE, *et al.*, 2014). Research on RO fouling has suggested biofouling is the most difficult fouling to prevent because biofilms can develop even if only a few cells are present, thus pretreatment cannot efficently prevent biofouling as in all other fouling modes through removal of a high percentage of constituents (KENT, FARAHBAKHSH, *et al.*, 2011, ZHENG, YU, *et al.*, 2018). It is anticipated that the fouling potential of the stream that feeds the RO in this Thesis is very low, since the FO membrane acts as a pretreatment, providing a barrier for the permeation of solutes even of low molecular weight, for example soluble microbial products, which are major causes of fouling. This observation, however, has only been proven experimentally proven so far by one work by LUO, Wenhai, PHAN, *et al.*, 2017.

In addition to fouling, issues related to the generation, management and disposal of retentates are also a valid concern (PIRAS, SANTORO, *et al.*, 2020). The sustainable management of RO retentate is the other major challenge to the implementation of RO in wastewater treatment and reuse and has been considered the most important limitation of using RO, as finding cost-effective rententate treatment technologies is a long-standing problem (JOO, TANSEL, 2015, KHAN, MURCHLAND, *et al.*, 2009). The composition of RO retentates include organic matter, refractory chemicals added by the public into wastewater (e.g., pesticides, personal care products, pharmaceutical products, endocrine disruptors), and residuals from wastewater treatment processes (e.g., soluble microbial products, partially biodegraded organics, anti-scaling chemicals) . In addition, membrane retentates may contain biological materials (i.e., bacteria, viruses, oocysts, and cell fragments) that also represent a potential environmental hazard (WESTERHOFF, MOON, *et al.*, 2009). For this reason, discharge of inadequately treated retentate could cause chemical pollution and ecotoxicity to the receiving water bodies, particularly as the concentration of pollutants in relation to feed quantity are higher (CAI, WU, et al., 2020, JOO, TANSEL, 2015).

In addition to the high ecotoxic potential, it must be considered that, in a context of wastewater teatment, the generated retentate is a process stream to be discarded and, therefore, it is subject to regulations that frame the quality required for its discharge in most countries. In Brazil, for example, the release into fresh surface waters is regulated by the regulation CONAMA 430 of 2011 (BRASIL, 2011). Therefore, treatment of retentate to decrease at least the overall chemical oxygen demand (COD) is usually necessary to meet legal discharge requirements.

Traditional management of RO retentates is mainly conditioned by the location of the plan; in coastal plants, surface discharge to marine environments is the simplest and most economical way of retentate disposal whereas in inland plants the traditional option consists on reducing the retentate volume prior to disposal, though this method has several disadvantages such as extensive land use and low productivity (CAI, WU, *et al.*, 2020, PÉREZ-GONZÁLEZ, URTIAGA, *et al.*, 2012). Existing technologies for retentate disposal have have been discussed comprehensively in recente reviews (CAI, WU, *et al.*, 2020, JOO, TANSEL, 2015, PÉREZ-GONZÁLEZ, URTIAGA, *et al.*, 2012, WESTERHOFF, MOON, *et al.*, 2009). Briefly, advanced oxidation processes (AOPs) have been standing out as effective alternatives for treatment of retentantes containing recalcitrant organic compounds. The use of such processes is logical because extensive treatment and energy inputs were spent to retentate the organics, and it is cheaper to treat smaller flowstreams (WESTERHOFF, MOON, *et al.*, 2009). It has also been proposed to combine AOP with a biological process, taking advantage of the fact that partial oxidation promoted by AOPs can produce biologically degradable material (e.g., organic acids) improving the performance of the subsequent biological process (CAI, WU, *et al.*, 2020, WESTERHOFF, MOON, *et al.*, 2009). More recently, retentate treatment in light of demands of removal of emerging pollutants started to be considered (ACERO, BENITEZ, *et al.*, 2016, JUSTO, GONZÁLEZ, *et al.*, 2013).

Pharmaceuticals removal

Another issue that has gained a lot of attention when discussing RO membrane technology is its removal efficiency regarding pharmaceuticals (PhACs) and, more generally, organic micropollutants. While in theory a total or near total removal of these compounds should be expected by the dense RO membranes (WARSINGER, CHAKRABORTY, *et al.*, 2018) by means of size exclusion and electrostatic repulsion, as previously mentioned, this is now recognized not to be true; as illustrated in Table 12, several PhACs usually at ng.L^{-1} levels can be found in RO permeate.

Table 12: Studies reporting micropollutants at ng.L^{-1} levels in permeate of reverse osmosis from MBR-NF/RO systems.

Micropollutants in RO permeate	**System**	**RO membrane material**	**Reference**
Benzotriazole, Metformin, Tramadol	MBR-RO-UV disinfection	Not informed by author. It is a commercial RO membrane, since this system is fully operational.	BUSETTI ET AL, 2015
Diclofenac, carbamazepine, bisphenol-A, triclosan, 4-octylphenol(4-OP),4- tert-octylphenol(4-t-OP).	MBR-RO	Polyamide	CARTAGENA ET AL, 2013
Acetaminophen, bisphenol A, carbamazepine, gemfibrozil, sulfamethoxazole, 17-α-ethinylestradiol, 17-ß-estradiol, estriol, estrone	MBR-RO	Polyamide	COMERTON ET AL, 2008
EDTA, naphtalene, estrone	MBR-RO	Polyamide thin-film composite	GARCIA ET AL, 2013
Erythromycin, sulfamethoxazole, Trimethoprim, acetaminophen, atenolol, carbamazepine, gemfibrozil, diazinon, diuron, mecoprop	MBR-RO	Polyamide	RODRÍGUEZ-MOZAZ ET AL, 2012
Estrone, atenolol, carbamazepine, diazepam, diclofenac, naproxen, fluoxatine, aspirin, acetaminophen	MBR-RO	Polyamide	RUEL ET AL, 2011
Cholesterol, salicylic acid, sulfamethoxazole, Trimethoprim	MBR-RO	Polyamide	SAHAR ET AL, 2011

Trimethoprim, sulfamethoxazole, bisphenol A, carbamazepine (NF permeate only)	MBR-RO	Polyamide	WANG ET AL, 2018
17β-Estradiol, Estriol, 17α-Ethinylestradiol	MF-RO	Polyamide	SILVA, 2016

The reasons for this permeation of PhACS through RO membranes can involve the geometry of these compounds, that does not facilitate the exclusion by size considering the free-volume (between polymer chains) of the active skin layer of the membrane; is also believed it involves complex relationships between hydrophobicity of solutes and the membrane, as previously discussed in this Chapter. This issue has been extensively reviewed by NGHIEM, FUJIOKA, 2016.

It is a matter of dispute whether there is need for concern for PhACs in such low levels in permeate when the permeate water is to be destined to high quality reuse, and therefore, whether further removals (here understood as below the detection level by high performance chromatography) are necessary, given the absence of specific guidelines for such situations. In this sense, a regulatory principle deserving consideration is the “precautionary principle”, which states that, when the scientific knowledge about risks can be persuasive, but not conclusive and unequivocal, it is important to be cautious in adopting an approach (MIAROV, TAL, *et al.*, 2020). The precautionary principle has been at the forefront of the management and assessment of risks in the fields of environmental protection and human health in the past two decades (MIAROV, TAL, *et al.*, 2020). The interpretation of this principle could be that, since hazards associated with presence of PhACs residues in ng.L^{-1} levels in treated effluents cannot, at this point of scientific knowledge, be proven or disproven definitively, one must move in the direction of precaution instead of discarding the potential hazard. Following these principle, the ideal target for PhACs removal from RO permeate should be as high as possible.

3.2.4 State of art of osmotic bioreactor integrated with reverse osmosis for wastewater treatment

As previously mentioned in item “Review of the OMBR literature and knowledge gaps” of this Chapter, only a small amount of works available about OMBR incorporate the stage of recovery of the DS by RO for production of reused water. To the best of the author knowledge there are only three reports that present a similar arrange to the one proposed in this Thesis i.e. assessing OMBR combined with RO for wastewater treatment and PhAC removal with the purpose of assessing water reuse: LUO, HAI, et al., 2016, LUO, PHAN, et al., 2017 and ZHANG, Bangxi, SONG, et al., 2017. It is noted that all the three works were developed by the same research group, based in Australia with contributions from groups in the United States and China, and present very similar experimental set-up, which were described in Table 10. The main results of these works are presented below.

In the work developed by LUO, HAI, et al., 2016, the performance of two ionic organic DS, namely sodium acetate (NaOAc) and ethylenediainetetra acetic acid disodium salt (EDTA-2Na) were compared to that of sodium chloride (NaCl) as DS for purposes of operating an OMBR-RO for water reuse. Each DS solution was prepared with a different concentration of salt so that they all had the same osmotic pressure of 23 bar. A cellulose-based FO membrane suplied by Hydration Technology Innovations was used. Results showed that NaCl and NaOAc reached the same initial water flux (6 LMH) while EDTA-2Na had an initial water flux of 4.5 LMH. However, EDTA-2Na had the lowest decrease in permeate flux during the operation, which at the end of 30 days was 22% , and therefore it was the DS that provided the highest water flux at the end of the experiment. NaCl water flux fell by 62% and NaOAC by 91% of after 30 days of operation. In all cases, membrane flushing was performed on days 10 and 20 of operation.

In regards to water quality, the type of DS had no influence on results: OMBR-RO could remove all 31 micropollutants investigated by over 97% regardless of DS. Besides, the use of NaOAc and EDTA-2Na reduced salinity build-up in the bioreactor in comparison with NaCl. Despite the lower RSF, the use of organic DS increased TOC concentration within the bioreactor compared to NaCl, mainly EDTA-2Na, which was ascribed to the high organic content of EDTA-2Na and its resistance to biodegration by activated sludge. Furthermore, because of the concentrated nature of the DS, when organic DS were used, the TOC concentration in recycled water (i.e. RO permeate) was higher than 10 $mg.L^{-1}$, which makes difficult to use this water for reuse and was probably the reason that the subsequent works by these authors used NaCl as DS, despite its much higher RSF.

Another interesting result of this work was the observation that, regardless of the DS employed, there was build-up of bulk organic matter and ammonium ($NH4^{+}$-N) in the DS. This type of result emphasizes the importance of studying the combined processes, since otherwise this result would not be quantifiable. The authors suggest an additional process, such as granular activated carbon adsorption, UV oxidation or ion exchange to address organic contaminant accumulation in the DS, allowing the production of high product water quality and sustainable operation of OMBR-RO in the closed-loop, but did not get to test any of these processes.

In the follow-up study by LUO, PHAN, et al., 2017, performance of OMBR-RO and conventional MBR-RO for wastewater treatment and reuse were compared. A TFC FO membrane made of thin, selective polyamide layer and a porous polysulfone support layer suplied from Hydration Technology Innovations was used in OMBR, and DS was NaCl 0.5M. Initial water flux yielded by this membrane was 13 LMH, thus considerably higher than that achieved by the cellulose-based membrane of the previous study. This flux, however, decreased by 53% after 20 days of continuous operation, with no membrane cleaning, which was attributed to both fouling and salinity build-up reducing the driving force of the process. Salinity build-up altered biomass characteristics and microbial community structure, resulting in release of more in more Soluble Microbial Products (SMP) and Extracellular Polymeric Substances (EPS) in the mixed liquor, further inducing the FO membrane fouling. A cake layer was observed on the membrane surface at the conclusion of OMBR operation, predominately consisting of carbon, oxygen, phosphorus, sodium, magnesium, and calcium, corroborating information from the literature that fouling is relevant in FO despite the absence of applied pressure. Moreover, this study also reported absence of fouling in the RO membrane due to the high rejection of FO membrane, being the only one in the literature so far to prove it experimentally, whereas in the MBR-RO system the fouling was severe in the RO membrane.

Considering the overall systems, no relevant differences regarding removal of bulk organic matter (i.e. TOC), micropollutants or nutrients (i.e. NH_4^+ and PO_4) were observed when comparing OMBR-RO and MBR-RO. The high rejection FO membrane resulted in negligible TOC concentration in the DS and thus ensured a complete overall removal by OMBR-RO. In MBR-RO, permeation of non-biodegradable dissolved organic substances through the MF membrane led TOC concentration in the bioreactor to be less than one-tenth of that in OMBR, but in return TOC accumulated in the MBR effluent reservoir. However, it was effectively retained by the RO membrane during all 40 days of operation, ensuring permeate without TOC. Regarding micropollutant removal, some of them (e.g.

primidone, atrazine, ametryn, diclofenac and carbamazepine) had low removals in MBR and high removals in OMBR; however, when considering the result combined with RO, the removals of all of them were equal and between 98-100%.

Effective nitrification also occurred in both bioreactors, which was measured by the decrease in NH4+. A limitation of this study is that it did not monitored nitrate, only total nitrogen (TN); the results showed considerable TN accumulation in the two bioreactors, in the DS and in the MBR effluent reservoir. Considering the measured reduction of NH4+, this TN accumulation was attributed to the nitrate that started to accumulate due to the absence of the denitrification stage given the aerobic conditions. This accumulation eventually led to a decrease in the removal in TN of both systems as a whole, from 100 to 50% in OMBR-RO and from 98 to 40% in MBR-RO in 40 days, i.e. there was possibly nitrate in the RO permeate.

The work of ZHANG, Bangxi, SONG, et al., 2017 compared the performance of the CTA and TFC FO membranes, both from Hydration Technology Innovations, in an osmotic membrane bioreactor (OMBR) using as DS NaCl 0.5M. A reverse osmosis (RO) system was integrated with OMBR to regenerate the draw solution and produce clean water that was analyzed for the presence of 31 micropollutants, TOC and nutrients.

Water fluxed reached by CTA and TFC membranes at startup were 6 and 8 LMH, respectively, and after 30 days of operations, both membranes yielded water fluxes of 3 LMH. The more dramatic flux decline in TFC membrane was attributed to a higher susceptibility of this membrane to organic fouling. Membrane autopsy revealed a more homogenous and thick cake layer in comparison with that on the CTA membrane. This was attributed to foulants transitioning from a sparse and loose fouling layer at a low initial permeate flux to a more compact and cohesive fouling layer at the higher initial permeate flux reached by TFC membrane. Moreover, TFC FO membrane was especulated to be more susceptible to organic fouling due to its membrane surface, with relatively higher roughness and prominent ridge-and-valley structure, making foulants deposited more easily shielded from air scouring or cross-flow shear force, thus facilitating the development of a cohesive fouling layer. A higher but subsequently lower salinity build-up in the bioreactor was also observed for OMBR using the TFC membrane compared to its CTA. Other results, however, were similar for TFC and CTA membranes:

when either was employed, RO permeate had no TOC; TN was in the range of 15 $mg.L^{-1}$ (because of the same rationale of the study of LUO, PHAN, *et al.*, 2017) and removal of micropollutants was between 98-100%.

High product water quality obtained by OMBR-RO in these three works suggests robustness of the process for water reuse applications. Nonetheless, due to the still very limited number of works available, these conclusions need further experimental validation, hence the motivation for this Thesis. Moreover, as no water quality parameter (TOC, nutrients, micropollutants) was considerably different from that obtained by MBR-RO, a conclusion could be that the greatest benefit of employing OMBR-RO would be to prevent fouling in the downstream RO process, thus reducing membrane cleaning and maintenance, and not in terms of water quality obtained. The fact that this was only mentioned in one paper emphasizes the importance of addressing this question in the present Thesis.

3.3 Materials and Methods

3.3.1 Draw solute selection

When selecting draw solutes in osmotic processes there is a tradeoff between small solute size solutes to limit ICP, thus maximizing water flux, or large solute size to decrease RSF, thus minimizing salinity build-up (SHAFFER, WERBER, *et al.*, 2015). In this Thesis, the criteria to select the draw solute was to prioritize a reduction in the salinity build-up in the reactor. This was based on the understanding that if the salinity in the reactor rises to very high values (higher than 15 mS/cm) in the short-medium term (up to 2 months), as has been widely reported in the literature (AFTAB, KHAN, *et al.*, 2015, GURUNG, CHRISTENSEN, *et al.*, 2020, SRINIVASA RAGHAVAN, QIU, *et al.*, 2018, TAN, Jia Ming, QIU, *et al.*, 2015, WANG, Xinhua, CHEN, *et al.*, 2014)), high salinity will impact heavily the process and may hinder feasibility of OMBR-RO. Such impacts include biological instability in the sludge with yet unpredictable effects on the removal of compounds and excessive operating cost due to frequent salt replenishment to compensate for the decrease in the driving force of the process, to name a few. Since it is known that salts with high diffusivity such as NaCl create high salinity build-up due to easier penetration through the FO porous layer, potassium pyrophosphate ($K_4P_2O_7$) was selected as draw solute because of its low diffusivity due to its large molecular size. A higher ICP was therefore expected due to the dilutive effect, resulting in less water flux, however this issue was addressed by increasing the membrane area. Other promising properties of $K_4P_2O_7$ for use as draw solute include high osmotic pressure, high solubility in water and absence of toxicity (CORZO, DE LA TORRE, *et al.*, 2017). Despite these characteristics, $K_4P_2O_7$ has not been tested as draw solute in OMBR systems so far.

DS was prepared by dissolving $K_4P_2O_7$ in deionized water (DI), obtaining a solution with osmotic pressure of 11 bar at 25 °C. On the 30th day of operation of the OMBR, DS conductivity was increased by adding $K_4P_2O_7$ to obtain an osmotic pressure of 21 bar, in order to compensate for the increase in conductivity within the bioreactor due to the salinity build-up. $K_4P_2O_7$ concentration was calculated using the relationship between conductivity and $K_4P_2O_7$ concentration according to the calibration curve in Figure 14, which was prepared before the beginning of the experiments. Osmotic pressure was calculated as a function of the calculated $K_4P_2O_7$ concentration, according the curve shown in Figure 15.

Figure 14: Calibration curve for potassium pyrophosphate.

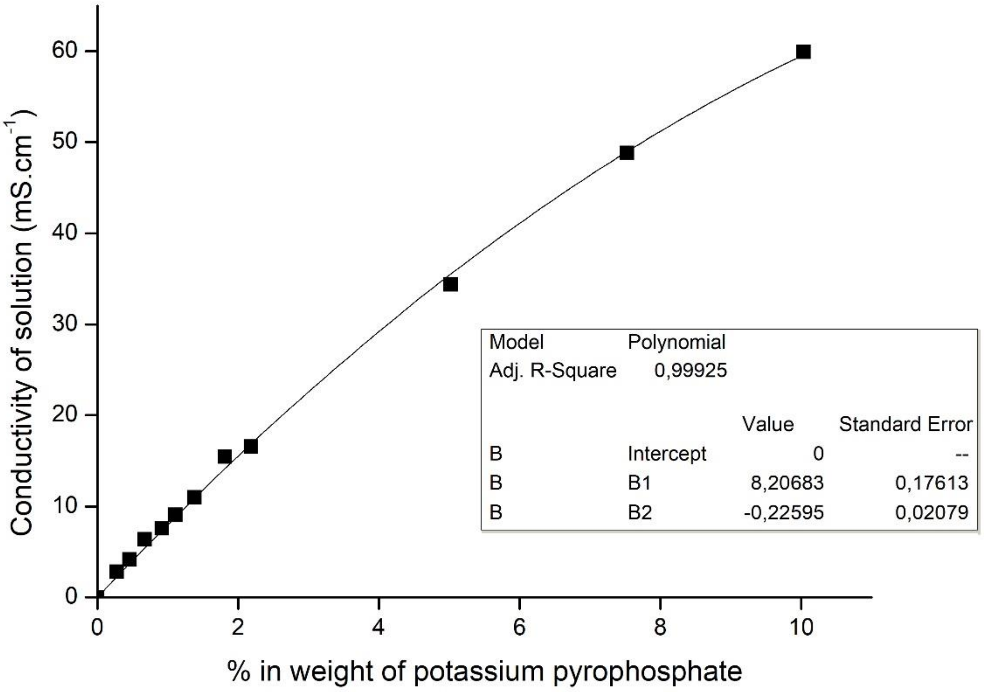
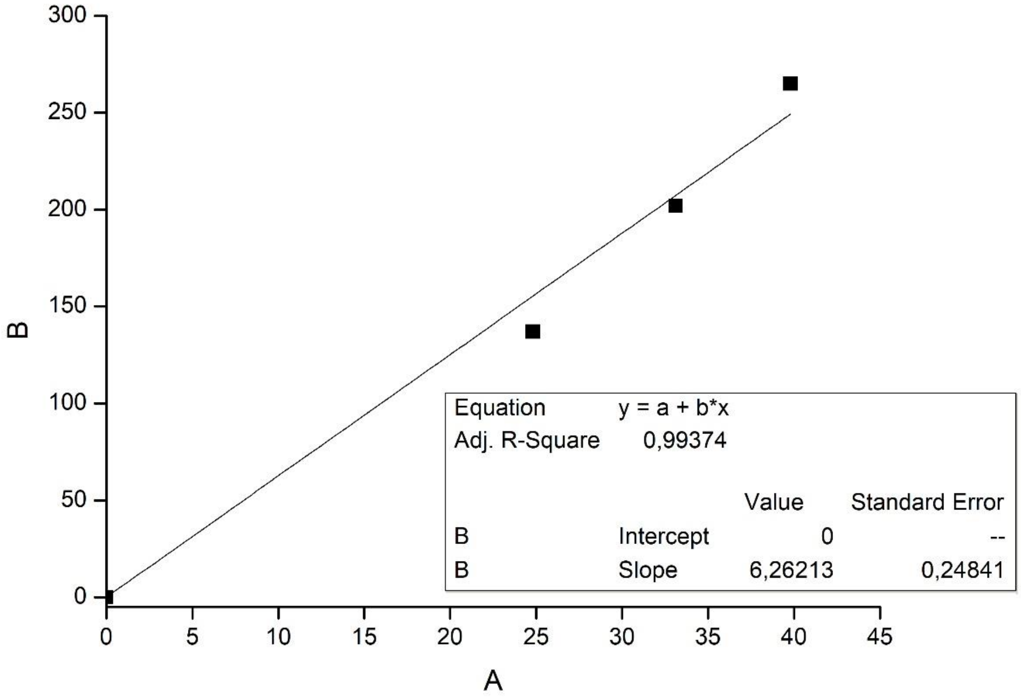


Figure 15: Osmotic pressure curve for potassium pyrophosphate.



*This curve was obtained by linear regression adjustment using data from (MICHAELS, JOHNSON, 1998).

3.3.2 Synthetic wastewater preparation

The influent water of the OMBR was synthetic wastewater containing PhACs. Its preparation and basic physical-chemical characterization have been described in Section 2.3.2. Further characterization is given in Table 13.

Table 13: Complementary characterization of synthetic feed wastewater

Parameter	Ammonium nitrogen (NH_4^+-N)*	60 ± 5 mg.L^{-1}
	Orthophosphate (PO_4^{3-})	79 ± 5 mg.L^{-1}
	pH	7± 0.2
	Ionic conductivity	850 ± 50 µS.cm^{-1}
Compounds (Pharmaceuticals)	Acetaminophen (ACT)	5.36 ± 1.89 µg.L^{-1}
	Sulfamethoxazole (SMX)	24.63 ± 4.59 µg.L^{-1}
	17-α-ethinylestradiol (EE2)	7.48 ± 0.96 µg.L^{-1}

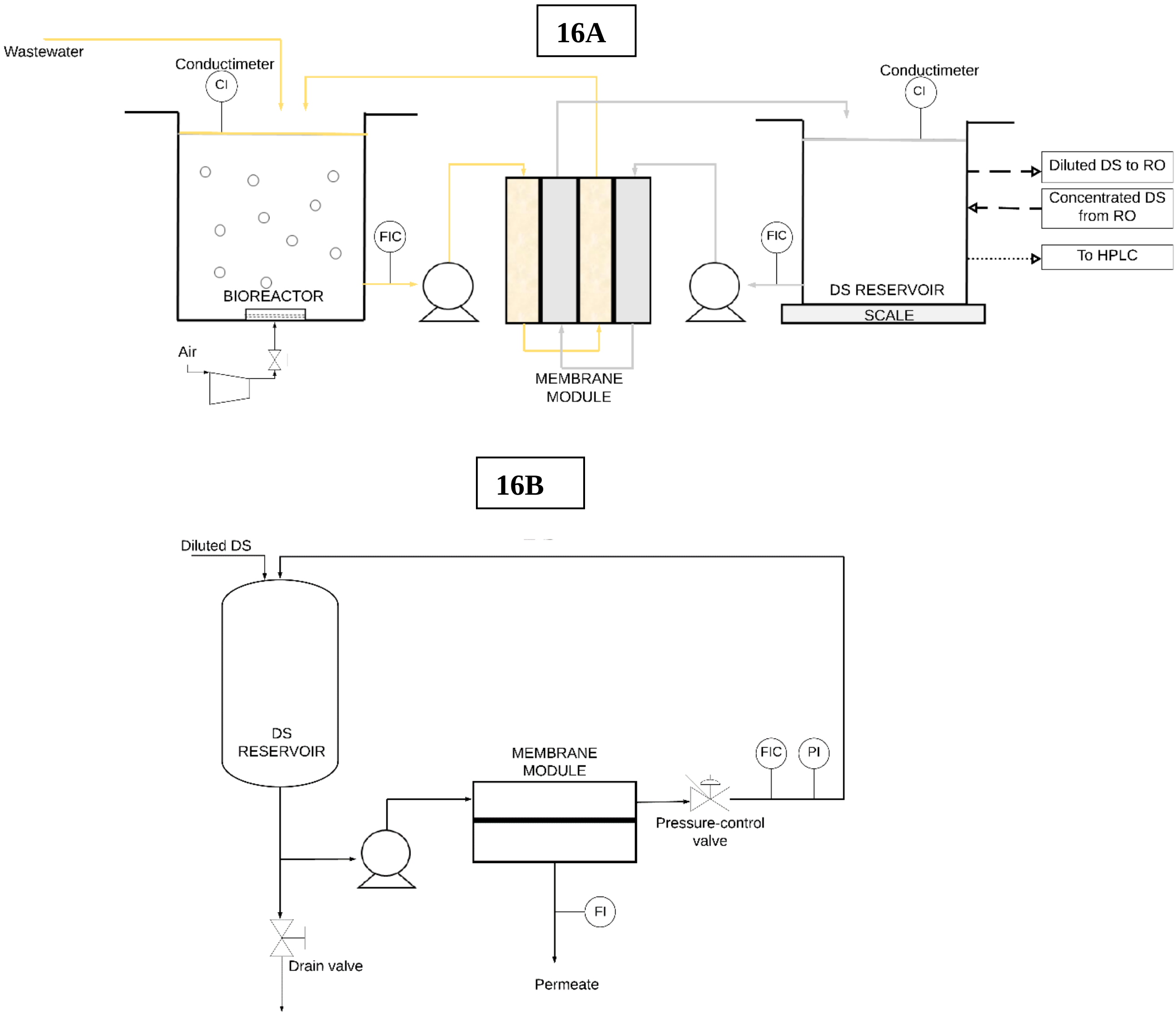
	Carbamazepine (CBZ)	14.53 ± 0.72 µg.L^{-1}
	Diclofenac (DIF)	12.76 ± 5.23 µg.L^{-1}

*measured at pH 7.0 and room temperature.

3.3.3 OsMBR and RO experimental setup

Figure 16 shows a scheme of the OMBR and RO laboratory scale systems.

Figure 16: Scheme of the experimental set-up, A) OMBR system in continuous operation and B) RO system for Draw Solution (DS) recovery and production of reclaimed water in batch operation.



*Dashed lines in 1A mean whenever DS conductivity dropped below the setpoint, DS was sent to RO for reconcentration and meanwhile it was replaced by previously reconcentrated DS. Dotted line in 1A means that in some predetermined periods of operation DS was not sent for recovery, but rather to HPLC analysis for PhAcs quantification.

The OMBR system (Figure 16A) contained an aerated bioreactor (1.0L) and DS reservoir (2.0L). The membrane module was a scalable plate-and-frame custom designed and fabricated in nylon containing three sheets of membrane, with a total effective area of 806 cm². Since this is a side-stream OMBR module, mixed liquor was used as feed solution (FS), and FS and DS were circulated at the flow rate of 1.0 $L.min^{-1}$ (Reynolds approximately 2100 at 25°C) from bioreactor/DS reservoir to the module and back. The active layer (AL) of FO membrane was placed to face the mixed liquor, as it is common in OMBR systems since if the porous support layer faces the mixed liquor, it gets clogged ((ADNAN, KHAN, *et al.*, 2019, LUO, Wenhai, PHAN, *et al.*, 2017, LUO, Wenhai, XIE, *et al.*, 2018, PATHAK, PHUNTSHO, *et al.*, 2020, TAN, Jia Ming, QIU, *et al.*, 2015)).

Freshly prepared synthetic wastewater was added daily to replace the exact volume extracted by the osmotic pressure difference through the FO membrane. Diluted DS was sent for recovery in reverse osmosis whenever its condutictivity fell below the value predetermined for the DS. To monitor the increase in conductivity inside the bioreactor and decrease of DS conductivity due to dilution, conductivity was daily measured in both mixed liquor and DS reservoirs.

Polyamide thin-film composites (TFC) flat sheet membranes (SR-90, Dow-Dupont, USA) were used for FO process by fixing three membrane sheets in-between plates. A low water flux was expected with this membrane, which was compensated by increasing the total membrane area since the objective of the study was specific to the evaluation of $K_4P_2O_7$ potential as DS and aplicability of OMBR-RO for the production of reclaimed water, and not evaluation of membrane properties and performance. Thus findings from this study are still valid using other FO membranes.

The RO system was used to reconcentrate the diluted DS and produce clean, reclaimed water. Figure 16B shows a scheme of the RO laboratory-scale system. RO membrane was a polyamide TFC sheet (SW30, Dow-Dupont, USA) mounted in a laboratory-scale cross-flow RO membrane cell made of stainless stell, with a flow channel height of 0.2 cm and an effective membrane surface area of 80 cm² (8x10cm). Key properties of RO and FO membranes are summarized in the Tables 14 and 15.

Table 14: Key properties of membranes used in this Thesis.

Membrane	Type	Test condition	Water permeability	Typical salt rejection	Reference
FO membrane (SR90 from Dow-Dupont)	Flat sheet, thin film composite	Experiments conducted in RO mode, feed at a constant temperature of 25 °C was either deionized water for permeance tests or a 2,000 mg/L $MgSO_4$ solution for rejection tests. Tests were conducted with feed pressure of 5 bar.	8.08 L/m².h.bar	99.6 % for $MgSO_4$	Manufacturer[8]
RO membrane (SW30 from Dow-Dupont)	Flat sheet, polyamide thin film composite	Experiments conducted in RO mode, feed at a constant temperature of 25 °C was either deionized water for permeance tests or a 2,000 mg/L NaCl solution for rejection tests. Tests were conducted with feed pressures of 55 bar.	0.75 L/m².h.bar	99.4% for NaCl	Manufacturer[9]

Table 15: Key physico-chemical properties of the selected pharmaceutically active compounds

Compound	Diclofenac	Carbamazepine	17-α-ethinylestradiol	Acetaminophen	Sulfamethoxazole

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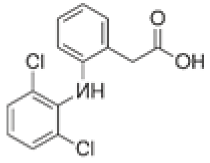
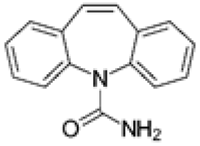
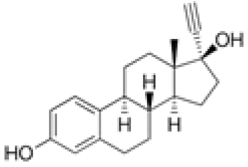
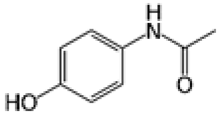
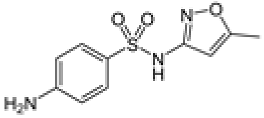
[8] Information from membrane data sheets sent by manufacturer: FILMTEC SR-90

[9] Information from membrane data sheets sent by manufacturer: FILMTEC SW-90

Molecular structure						
Formula		$C_{14}H_{11}NCl_2O_2$	$C_{15}H_{12}N_2O$	$C_{20}H_{24}O_2$	$C_8H_9NO_2$	$C_{10}H_{11}N_3O_3S$
Molecular weight (g/mol)		296[c]	236[d]	296[d]	151[d]	253[d]
pKa		4.2[a]	13.9[a]	10.7[b]	9.3[a]	5.2[a]
log Kow		4.51[c]	2.45[d]	3.67[d]	0.46[d]	0.89[d]
Charge at pH 7		negative	neutral	neutral	neutral	negative
Charge at pH 9		negative	neutral	neutral	neutral	negative
Molecular dimension	Width (Å)	9.1[c]	5.7[d]	5.7[d]	5.3[d]	5.6[d]
	Length (Å)	11.3[c]	9.5[d]	11.9[d]	8.0[d]	12.9[d]
	Volume ($Å^3$)	Not available	693.3[d]	881.1[d]	492.1[d]	702.8[d]

[a] Source: (JANG, Duksoo, JEONG, *et al.*, 2018)

[b] Source: (COMERTON, ANDREWS, *et al.*, 2008)

[c] Source: (VERGILI, 2013)

3.3.4 Coupling of OMBR-RO

Whenever conductivity of DS, which was continuously circulated inside the OMBR system fell below the predetermined value, the process was interrupted briefly to allow the DS replacement by DS previously reconcentrated by the RO system. Thus there were 2 DS solutions simultaneously in use, one being circulated in OMBR and another being recovered by RO. It is noted, however, that in seven periods, equally spaced throughout the operation time, freshly prepared DS was used and, at the end of the predetermined period, it was sent directly for HPLC analysis in order to evaluate experimentally the extention of solute accumulation in DS.

3.3.5 OSMBR-RO operating conditions

The OMBR was continuously operated for 52 days. Mixed Liquor Suspended Volatile Solids (MLVSS) was initially set at 2.66 $g.L^{-1}$, using the seed sludge acclimated to PhACs collected on the 170th day of operation of conventional activated sludge bioreactor described in Chapter 2. Hydraulic Retention Time (HRT) was set inially at 48h and increased with time as the flux of FO decreased.

In practice, salinity build-up in the bioreactor can be alleviated to some extent by regular sludge wastage, however in this study, no sludge was wasted to systematically investigate salinity build-up in the OMBR when using $K_4P_2O_7$. Dissolved oxygen (DO) concentration was kept at approximately 5 $g.L^{-1}$ to allow nitrification to happen, as the two steps in nitrification require strongly aerobic conditions, thus requiring stronger aeration than employed in usual operation (MANAHAN, 2000).

RO was carried out under operating hydraulic pressure of 30 bar. Prior to the experiments, the membrane was compacted at 30 bar until constant water flux was obtained. During recovery of DS, permeate flux was measured every 15 minutes; when the permeate volume was equivalent to the volume of water extracted in OMBR stage, the experiment was considered concluded. The same RO membrane was used throughout the entire bioreactor operation time, with no cleaning between one DS recovery experiment and the next.

3.3.6 Control bioreactors

Control bioreactors 1 and 2 were operated continuously and in parallel to the OMBR. Their startup was on the same day and using the same sludge inoculum as the OMBR. Operating conditions in the controls were also the same than in OMBR (Dissolved oxygen 5 $mg.L^{-1}$, complete sludge retention, mixed liquor volatile suspended solids around 2.5 $g.L^{-1}$). Control 1 and 2 were conventional activated sludge bioreactors with suspended biomass and separation of the supernatant by gravity decantation. The volume of supernatant removed daily was equivalent to that which had been extracted by FO at OsMBR in the same period, so that the same volume of fresh synthetic wastewater that was added to the OMBR was also added to the controls.

The purpose of the operation of these controls was to allow a separate investigation of two different effects (salinity and presence of PhACs) on the biological activity of biomass. In the case of control 1, the synthetic wastewater used to replace the supernatant was the same as in OMBR (described in section 2.3.2) and no $K_4P_2O_7$ was added, so the conductivity of this mixed liquor remained in the range of 850 ± 50 $\mu S.cm^{-1}$. In the case of control 2, the synthetic wastewater used to replace the supernatant was the one from described in section 2.3.2 but without addition of standard solution containing the pharmaceutically active compounds (PhACs) sulfamethoxazole (SMX), carbamazepine (CBZ), diclofenac (DIF), 17-α-ethinylestradiol (EE2) and acetaminophen (ACT). Furthermore there was daily addition of $K_4P_2O_7$ in order to accompany the increase in the conductivity of mixed liquor in OMBR.

3.3.7 Membrane bioreactor and reverse osmosis system

20 L of biologically treated effluent obtained by the operation of the activated sludge bioreactor described in Chapter 2 were collected at the end of the operation of that bioreactor (on the 170th day). A biocide (sodium azide 100 $mg.L^{-1}$) was added to interrupt any remaining biodegradation and the effluent was microfiltered using a pilot system containing two hollow-fiber modules with microfiltration membranes made of polyetherimide (PAM Membranas®), with an average pore size of 0.4 µm.

MBR permeate was collected and 2L were analyzed by chromatography to quantify the PhACs; the remaining volume (8L) was taken to the reverse osmosis (RO) system outlined in Figure 16B. A hydraulic pressure of 30 bar and a 50% permeate recovery were applied in RO system. A new membrane, equal to the one used in the RO experiments for recovery of draw solution (DS) (polyamide TFC sheet SW30 from Dow-Dupont, USA) was introduced in the RO cell prior to this experiment, and it was compacted with hydraulic pressure of 30 bar at constant pressure prior to the experiment. The RO permeate obtained was analyzed to quantify the PhACs. The objective was to compare the quality of the water obtained by this MBR-RO with that obtained by the OMBR-RO system evaluated in this Thesis.

3.3.8 Analytical Methods

Water and salt flux measurement

Experimental water flux J_w ($L.m^{-2}.h^{-1}$ or LMH) and reverse salt flux J_s ($g.m^{-2}.h^{-1}$ or gMH) were determined using Equation 28 and 29, respectively:

Equation 28

$$J_w = \frac{\Delta V}{A \,. \Delta t}$$

Equation 29

$$J_s = \frac{V_t \,. C_t - V_{t-1} C_{t-1}}{A \,. \Delta t}$$

Where ΔV is the net increase in the diluted DS volume (L), calculated by measuring the weight variation of DS over a time interval Δt (h), Vt is the volume of $K_4P_2O_7$ solution at time t, Ct is the concentration of $K_4P_2O_7$ at time t and A is effective area of FO membrane (m^2). The calibration curve (Figure 14) was used to obtain the $K_4P_2O_7$ concentration.

Solute permeability measurement

The solute permeability (B) is the proportional constant of solute transport through a membrane, which is solute-dependent and can be calculated using Equation 30 (KIM, Bongchul, GWAK, *et al.*, 2017):

Equation 30

$$J_s = B.\Delta C$$

where ΔC is the solute concentration difference between the two sides of a membrane.

Solute permeability through the FO membrane was calculated for $K_4P_2O_7$ as the slope of curve Js versus concentration difference between the feed (mixed liquor) and DS, which were measured daily during OMBR continuous operation.

Before the start of the operation of OMBR, solute permeability was also calculated for $K_4P_2O_7$ and for NaCl in preliminary experiments using the same FO system (Figure 16A), DI water as feed and known concentrations of salt in the DS. The duration of these experiments was 6 hours.

Solute permeability through the RO membrane was calculated for PhACs considering the concentration difference between RO feed and permeate, both measured by SPE-HPLC, and the permeate flux measured experimentally.

Basic water quality parameters

Dissolved Organic Carbon (DOC), Chemical Oxygen Demand (COD), 5-day Biological Oxygen Demand (BOD_5), turbidity, true color, pH, Oxygen Uptake Rate (OUR), MLVSS, ionic conductivity, nitrate, nitrite and ortophosphate were determined in agreement with the standard procedures(APHA/AWWA/WEF, 2012). Dissolved organic carbon (DOC) was analyzed in DOC analyzer (Shimadzu, Kyoto) and nitrate and phosphate were analyzed using colorimetric kits (Sigma Aldrich, Brazil).

Analysis of pharmaceutically active compounds

PhACs were analyzed on reclaimed water samples (RO permeate of the OMBR-RO and MBR-RO systems) and also on diluted DS samples, after recirculation in OMBR for a predetermined period. PhAcs analysis followed the method previously described in Chapter 2 in section PhAC analysis.

Diluted DS samples were acidified to neutral pH using HCl 3M prior to SPE, due to the the strong alkaline character of solutions containing $K_4P_2O_7$ and the requirements for operating both the cartridges and the C-18 column in the neutral pH range. During method validation, it was verified that the presence of $K_4P_2O_7$ in the solution did not affected method recovery, linearity, quantification and detection limit, therefore, the method was considered valid for analysis regardless of the presence of $K_4P_2O_7$.

Since the permeate sample was diluted with the initial DS, the initial and final DS mass for each experiment were measured, and concentrations obtained by SPE-HPLC analysis were corrected to correspond only to the volume that permeated the membrane i.e. OMBR permeate. It is noted that as water flux permeating through the FO membrane continuously decreased over the operating time, there was increasingly less volume corresponding to OMBR permeate in the diluted DS. To compensate for this, samples collected after the 3rd operation week were spiked with a standard solution containing the five PhACs, whose concentration was discounted in the final calculation. The difference, if any, between the value measured in the sample and the value spiked was considered the concentration of PhAc in the original sample (ALTURKI, Abdulhakeem, MCDONALD, *et al.*, 2012b, WISCONSIN, 1996).

3.4. Results and Discussion

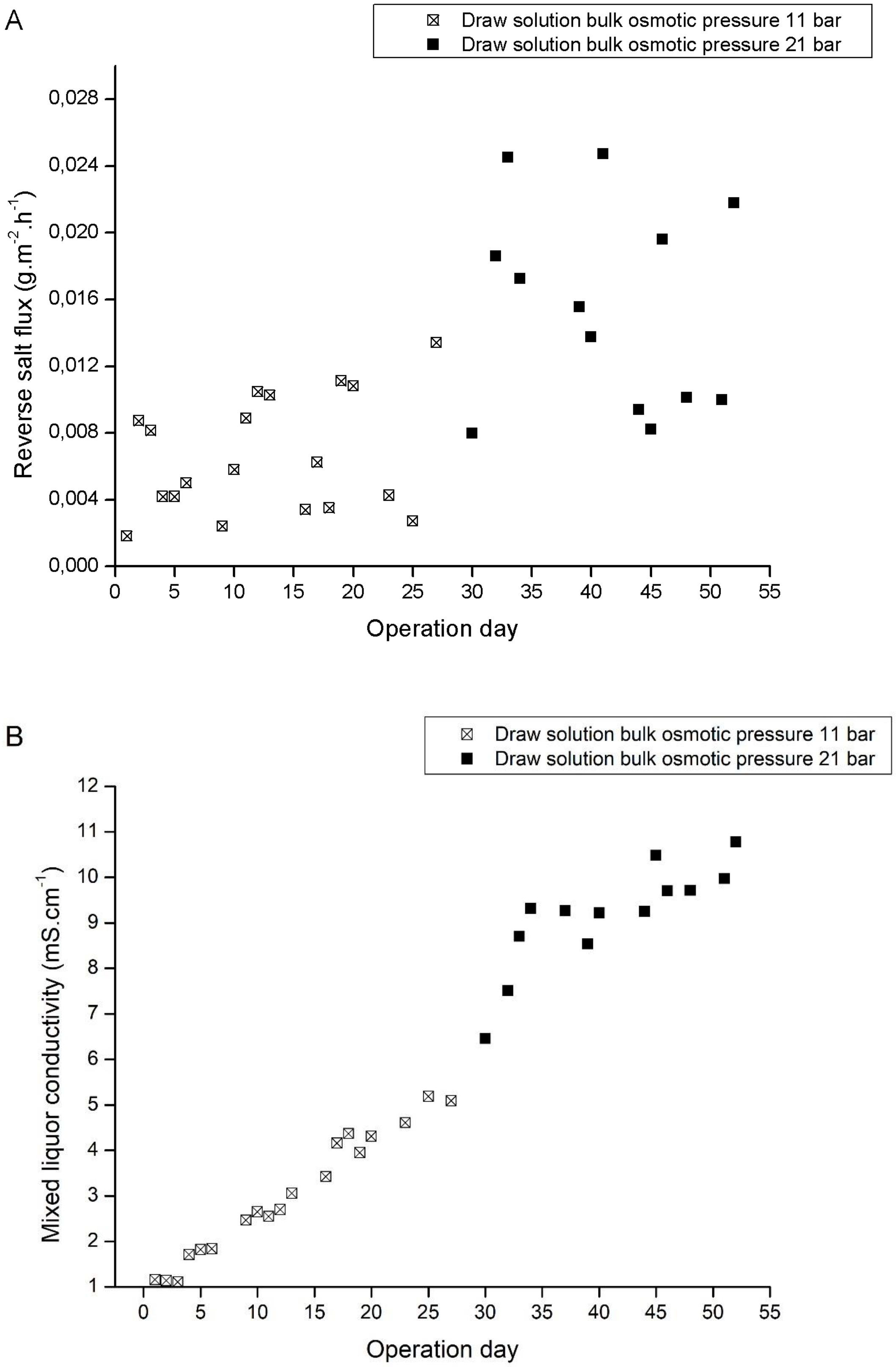
3.4.1 Osmotic membrane bioreactor operation

A continuous OMBR experiment was conducted to preliminarily assess the process performance when employing $K_4P_2O_7$ solution as innovative draw solution. Preliminary assessment was made in regards to reverse salt flux/solute permeability and to biomass biological activity, given that those issues are key challenges in OMBR technology (BLANDIN, LE-CLECH, *et al.*, 2018, HOLLOWAY, ACHILLI, *et al.*, 2015, WANG, Xinhua, CHANG, *et al.*, 2016).

Reverse solute flux and permeability

Figure 17 presents the reverse salt flux (RSF) from DS to the mixed liquor.

Figure 17: Variation of A) reverse salt flux and B) mixed liquor conductivity during OMBR operation.



OMBR was operated for 52 days and during the first 30 days, DS bulk osmotic pressure was maintained at 11 bar. There was salinity build-up in the bioreactor in this period (Figure 17B), which can be attributed both to the retention of solutes from the feed by the FO membrane and the reverse diffusion of $K_4P_2O_7$ from the DS (GURUNG, CHRISTENSEN, *et al.*, 2020, ZHANG, Bangxi, SONG, *et al.*, 2017). To compensate for this salinity build-up, DS bulk osmostic pressure was increased to 21 bar on day by adding $K_4P_2O_7$. With higher $K_4P_2O_7$ concentration, there was a greater increase in. This led to the increase observed in the RSF and thus in mixed liquor conductivity by enhanced $K_4P_2O_7$ diffusion through the FO membrane from this day on, since the osmotic pressure difference across the membrane is the driving force for the transport of draw solute. This relationship between the increase in DS osmotic pressure and higher RSF has been reported by other authors (CORZO, DE LA TORRE, *et al.*, 2017, KIM, Bongchul, GWAK, *et al.*, 2017, LUO, Wenhai, HAI, *et al.*, 2015).

RSF depends on the driving force (i.e. concentration gradient) existing across the membrane. As the OMBR literature mostly uses NaCl solution as DS, with concentrations higher than the used in this work, for comparison purposes the salt permeability (B) is preferred. B is important to quantify the mass of salt being permeated to the mixed liquor for a given fixed experimental condition, and was obtained experimentally for the period in which the osmotic pressure was fixed at 11 bar as 0.05 LMH. This value is considerably lower than those reported in the review paper by Kim et al. 2017 (KIM, Bongchul, GWAK, *et al.*, 2017), which was in the range of 0.11-1.75 LMH for NaCl solution as DS. The lower permeability of $K_4P_2O_7$ in this work can be attributed to its slow diffusivity and high rejection by size of the FO membrane. In comparison, the rejection of FO membrane to NaCl is much smaller, because chloride is a smaller anion, making NaCl highly diffusive. This is illustrated in Table 16.

Table 16: Solute flux (Js), solute permeability (B) and salt rejection for the FO membrane used in this study, NaCl and $K_4P_2O_7$ as draw solution.

Draw solution	**Molar concentration (M)**	**Osmotic pressure, bar**	**Reverse salt flux, $g.m^{-2}.h^{-1}$***	**Salt permeability (B), $L.m^{-2}h^{-1}$***	**Salt rejection (%)****
$K_4P_2O_7$	0.3	64	0.0061	0.000061	98.3%
NaCl	1.2	64	16.900	0.241420	29.9%

*solute flux and permeability measured by FO system shown in Figure 16A. Experimental conditions of the FO tests: room temperature, feed side DI water, total duration of each experiment 6h.

**Salt rejection measured by RO system shown in Figure 16b. Experimental conditions of the RO test: applied pressure 30 bar, room temperature, concentration of salt in the feed of 2,000 part per million (ppm).

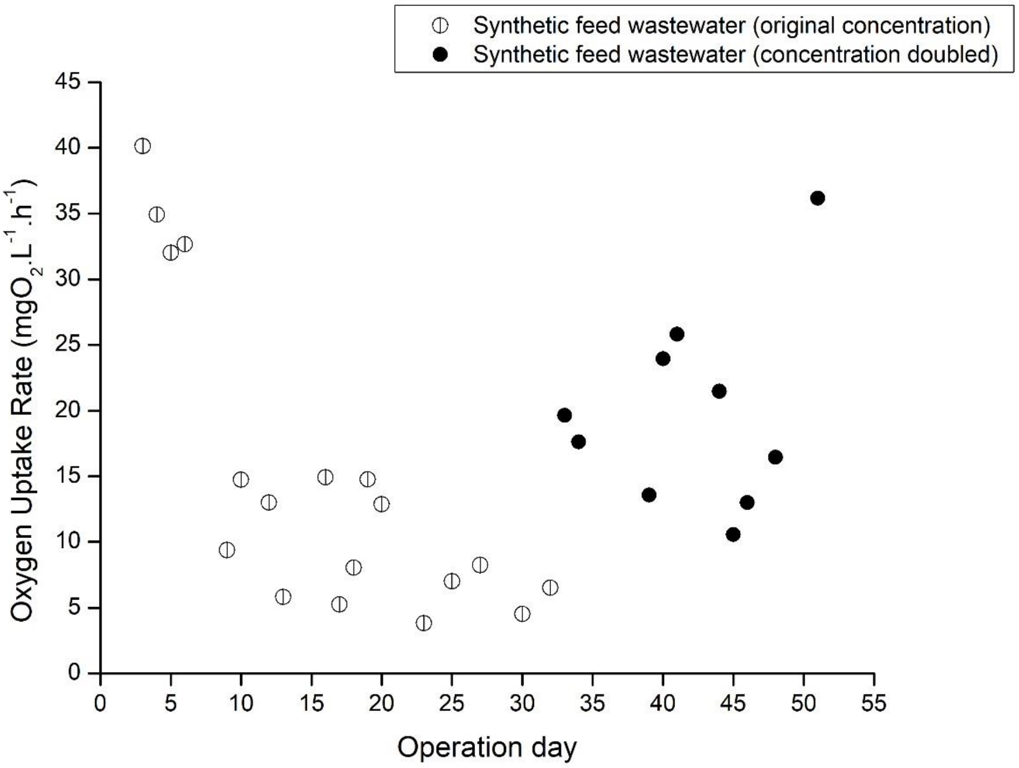
Pure water permeability (A) was obtained experimentally in preliminary tests with OMBR system as 0.040 $L.m^{-1}.h^{-1}.bar^{-1}$ ($LMH.bar^{-1}$), a value that was maintained at the startup of the bioreactor. This low permeability was expected due to the characteristics of the porous layer of the FO membrane used, which includes non-woven paper. Parameter S, which describes the characteristics of the porous layer, should be minimized and is usually around 500 µm in common FO membranes (ALSVIK, HÄGG, 2013, XIE, NGHIEM, *et al.*, 2014), but is in the order of 37500 µm for commercial membranes similar to the one used in this study with non-woven support (ALSVIK, HÄGG, 2013), which shows the propensity of this membrane to Internal Concentration Polarization (ICP). This low water flux was circumvented by increasing membrane area in the OMBR, which impacts the process performance only in terms of a higher mass flow of salt transferred to the mixed liquor, since there is more membrane in contact with the liquor. It is noted, however, that RSF remained very low, as shown in Figure 17A, so this increase in area did not impact the conclusions regarding the use of $K_4P_2O_7$.

TFC membranes used in the OMBR literature are much more restrictive to the passage of NaCl than the FO membrane used in the present work, with at least 90% NaCl retention, and yield higher water flux, thus requiring less membrane area per volume of treated effluent (YIP, TIRAFERRI, *et al.*, 2010, ZHANG, Bangxi, SONG, *et al.*, 2017). Besides, sludge wastage, which helps alleviating salinity build-up, was not done throughout the operation. Thus, it is expected that when using FO membranes more restrictive to salt and wasting sludge, solute permeability and RSF will be even lower than that obtained in this study, which higlights the potential of $K_4P_2O_7$ solution as DS to reduce RSF in OMBR.

Biomass biological activity

Since $K_4P_2O_7$ solution has not yet been assessed as DS in an OMBR, it was necessary to prove whether, and if so to what extent, its presence in the mixed liquor affected the biomass. Biological activity was assessed by means of oxygen consumption (measured as OUR) and by biomass growth (measured as the difference of measured MLVSS). Notable changes in both parameters were observed during the continous OMBR operation. Figure 18 shows there was a downward trend in the aerobic activity measured by OUR over the initial weeks of operation.

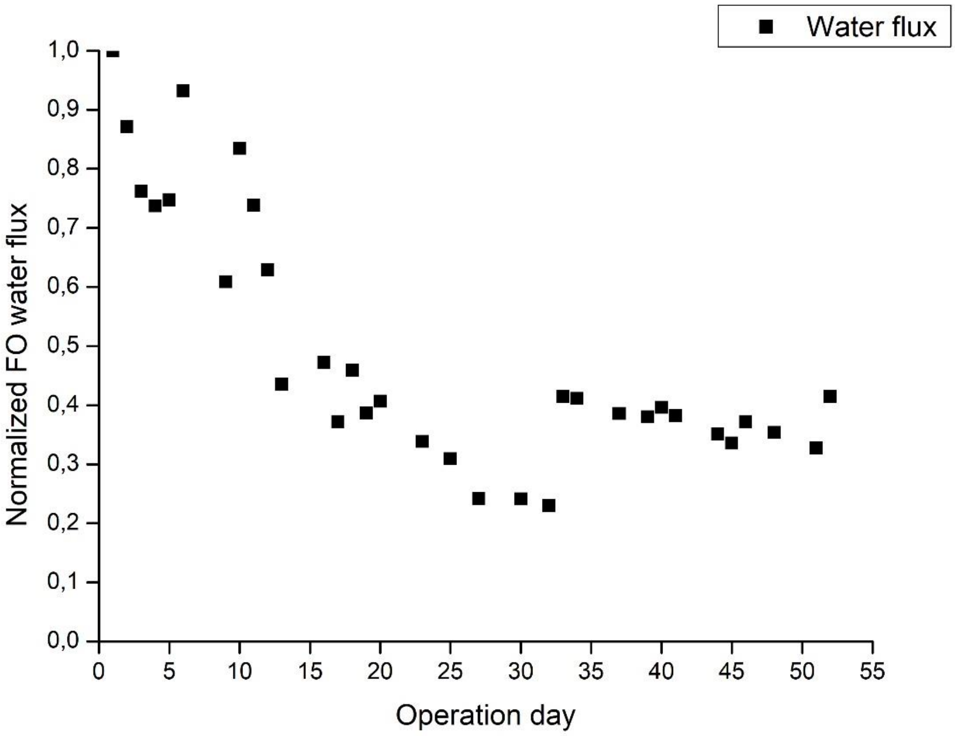
Figure 18: Oxygen Uptake Rate (OUR) measured in the OMBR mixed liquor throughout the continuous operation of OMBR.



*Original concentration refers to that described in section 2.3.2.

The decrease in OUR coincided with a decline in OMBR water flux (Figure 19). Water flux decline can be attributed mainly to membrane fouling and salinity build-up in the bioreactor, which reduces the effective driving force (i.e. transmembrane osmotic pressure) for water transport (NGUYEN, CHEN, *et al.*, 2015, ZHANG, Bangxi, SONG, *et al.*, 2017).

Figure 19: : Normalized FO water flux measured throughout the continuous operation of OMBR.



A condition that may have influenced the OUR decline was that less influent was introduced into the reactor with each passing day and, accordingly, less organic matter and nutrients were available for the microorganisms. This happened because the volume of influent introduced every day in the OMBR was calculated to replace the water extracted by the osmotic process, which decreased daily (Figure 19). To test the influence of a smaller input of organic matter and nutrients over the process, a change was made to the composition of the original synthetic feed wastewater (described in section 2.3.2) on the 32nd day of operation. The modification consisted of doubling the original concentration of each component, except the PhACs, thus providing twice as much organic matter and nutrients. From day 32 forward, there was a trend of increase in OUR, showing that the lowering of OUR was associated primarily with biomass starvation and not other possible factors, for example, salinity build-up. This is further corroborated by the observation that mixed liquor conductivity was higher in the last weeks of operation than in the initial weeks (Figure 17B) and yet there was a clear trend of increasing OUR in the last weeks of operation. Therefore, salinity did not impact diretly biomass oxygen consumption.

As observed in Figure 19, there was an improvement in FO water flux from day 32 on, even though no cleaning was made on the FO membrane. This increase may be attributed to the increase in DS osmotic pressure from 11 to 21 bar, which was done to compensate for the salinity builudp in the bioreactor, as previously mentioned, and which had the effect of increasing the net driving force for water flux according to Equation 22. Furthermore, it is possible that there was a lower release of organic compounds that cause fouling once the starvation situation has been corrected, thus contributing to higher water flux. This is because it has been experimentally proven that, under starvation conditions, there is large leakage of organic compounds from cell lysis and subsequent degradation of dead bacteria, and those compounds are mostly large (with molecular wight above 10 kDa), which also creates remarkable fouling in submerged membranes (PALMARIN, YOUNG, *et al.*, 2020, ZHANG, Hai Feng, SUN, *et al.*, 2009).

The initial FO water flux was 0.43 $L.m^{-2}.h^{-1}$ and there was a 58.5% decline in this flux at the end of 52nd day of operation. Such % decline is in accordance to values in literature for OMBR using FO membranes with similar active layers materials than the one of this study: total decline of 66.67% after 30 days of operation (ZHANG, Bangxi, SONG, *et al.*, 2017) and 42.85% after 20 days (GURUNG, CHRISTENSEN, *et al.*, 2020) have been reported, all without cleaning of membrane.

Unlike OUR, biomass growth was affected by OMBR operating conditions, as shown in Table 17. There was a 67.27% decline in MLVSS after 52 days of operation, even with complete retention of these solids within the reactor, obtained by the FO membrane retention and no sludge wasting.

Table 17: Parameters related to biological aerobic activity in the beginning (1st) and end (52nd) of operation of OMBR and control bioreactors, all subjected to same experimental conditions.

Parameter	Bioreactor	Beginning	End
OUR ($mgO_2.L^{-1}h^{-1}$)	Control 1	38.35	41.62
	Control 2	36.13	31.33
	OsMBR	40.14	36.16
MLVSS ($mg.L^{-1}$)	Control 1	2.60	3.55
	Control 2	2.59	0.61
	OsMBR	2.66	0.87
SOUR ($mgO_2/gMLVSS.^{-1}h^{-1}$)	Control 1	14.75	11.72
	Control 2	13.95	51.36
	OsMBR	15.09	40.41

The effect observed on biomass growth in the OMBR can be attributed to salinity and/or accumulation of solutes in mixed liquor at concentrations that become toxic to biomass due to high retention by the FO membrane. For example, the PhACs added to the influent wastewater stand out as compounds that can affect biomass when their concentration increase in mixed liquor, especially those recognized for their low biodegradability and toxic potential in higher concentrations such as CBZ (HAI, YANG, *et al.*, 2018). To investigate which of the two phenomena was responsible, two control reactors, represented by controls 1 and 2 in Table 17, were operated after inoculation with the same sludge previously acclimated to PhACs. MLVSS values at the end of OMBR operation shows that the biomass of OMBR and of control 2 did not grow as would be expected under normal operation conditions, represented by control 1. Furthermore, as the final values obtained in the OMBR and control 2 are similar, the low MLVSS growth may be associated with increased salinity and not with an eventual increase in PhACs concentration in the mixed liquor created by the retention of the FO membrane to these compounds, since no PhAcs were added to influent wastewater of control 2 and biomass growth in this reactor was still affected. Therefore, salinity can be attributed to the observed growth inhibition.

Low biomass growth in OMBR submitted to conditions of high salinity has also been reported in literature: Luo et al. (LUO, Wenhai, HAI, *et al.*, 2015) reported a 20% drop in MLVSS after 14 days of operation using NaCl as DS, Adnan et al. (ADNAN, KHAN, *et al.*, 2019) found a 50% drop in MLVSS after 17 days of operation with ammonium sulfate salt as DS, and Wang et al. (WANG, Xinhua, CHEN, *et al.*, 2014) found a 91% drop in MLVSS after 40 days of operation with NaCl as DS. These authors attributed the inhibition of growth to the inability of biomass to adapt to the saline condition. It has been recognized that increasing salt concentration results in slower microbial kinetics, with lower growth yield coefficient (Y) and higher endogenous decay or death rate coefficient (LAY, LIU, *et al.*, 2010). The problems created in biomass due to increased salinity are related to osmotic stress on the microorganisms generated by the osmotic pressure of the environment, that causes an outward flow of intracellular water, resulting in cell dehydration and eventually, plasmolysis and loss of cell activity (LAY, LIU, *et al.*, 2010). Therefore, the problems do not arise of the nature of the salt but rather on the osmotic pressure created by its presence, so the results of this work in terms of growth inhibition are consistent with the literature despite the different salt used.

Since less biomass was present in the mixed liquor at the end of the experiment, but the OUR had already recovered the original value, the SOUR of the osmotic reactor at the end of the operation was much higher than at the beginning (Table 17). Increase in SOUR in OMBR has been previously reported (WANG, Xinhua, CHEN, *et al.*, 2014). The reason why oxygen consumption (OUR) at the end of the operation was close to that obtained at the beginning without salinity, but the amount of biomass was not, may be related to the way microorganism metabolism responds to osmotic stress. In studies with bacterial isolated colonies, it is observed that the response to chemical stress demands a lot of carbon and energy resources, thus shifting the tight coupling that usually exists between catabolism (substrate utilization) and anabolism (growth related biosynthesis) towards catabolism (KATARIA, RUHAL, 2014, RAY, PETERS, 2008). Consequently the biomass growth yield decreased in these colonies while substrate utilization rates, as indirectly measured by OUR were not inhibited, which was also reported in this work. These microbial mechanisms need to be further studied for the specific case of OMBR biomass to prove this conclusion, which is outside the scope of the present work. However, if proven, it would show that a low biomass growth does not represent insufficient acclimatization to the saline condition but rather an adaptation of the bacterial metabolism to the presence of salinity. In this case, it would be possible to achieve effective biological operation in OMBR but with less sludge production for disposal than in conventional aerobic biological processes, which represents a valuable advantage of OMBR, since the large sludge production in these conventional processes is one of their greatest disadvantage.

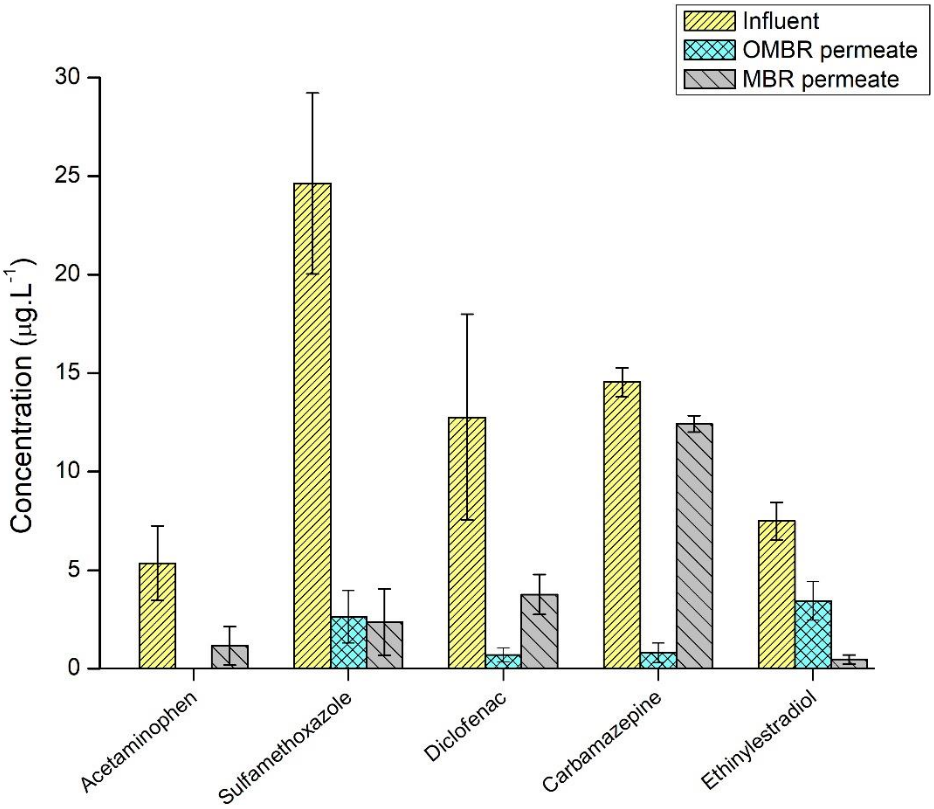
3.4.2 Pharmaceutical permeation to diluted draw solution

The mixed liquor contains a relatively high concentration of several solutes, including PhAcs, whereas DS at first does not have concentration of these components. Therefore, a concentration gradient is created and these solutes were expected to permeate by diffusion through the FO membrane moved by this gradient, according to Equation

30, to a extent limited by their diffusivity in the membrane material. This permeation was confirmed by HPLC analysis of the draw solutions.

During the 52 days of continuous operation, there was an alternation between draw solutions that were recovered at the RO stage (for the production of reuse water) and the draw solutions that were in contact with the mixed liquor for 72h and then sent to analysis by HPLC. A total of 7 DS were analyzed by HPLC, and the results of these analyzes are shown in Figure 20. The Figure also shows results of PhACs concentration in the permeate of conventional MBR.

Figure 20: Pharmaceutically ative compounds concentration in the influent that feeds both the OMBR and MBR and in the OMBR and MBR permeate.



*Error bars represent standard deviations (n=7).
**Acetaminophen was below method quantification limit (3 ng.L^{-1}) in all OMBR permeate samples.

The immediate implication of PhACs permeation, considering the applicability of the combined OMBR-RO process for water reclamation, is that the concentration of PhACs in diluted DS will continue to rise in the medium term operation (>72h); since the diluted DS is reconcentrated by the subsequent RO in a cloosed-loop (as illustrated in

Figure 1), increasing the concentration in the diluted DS i.e. RO feed may eventually impact the water quality of the RO permeate. This accumulation of solutes in the DS has already been predicted in simulations of FO-RO systems (D'HAESE, LE-CLECH, *et al.*, 2013, PHUNTSHO, KIM, *et al.*, 2017). However, the experimental results of this Thesis prove, for the first time, that permeation and consequently accumulation occurs in non-negligible concentrations (µg.L^{-1}), which are in the same order of magnitude of the OMBR influent wastewater, after 72h of continuous contact between mixed liquor and DS. It is noteworthy that these observations may only arise from the analysis of the combined processes, where aspects of the first one affect the subsequent one, reinforcing the need to study the combined processes to assess the real applicability of the OMBR-RO for water reclamation and hence the justificative for this Thesis.

The impact of this result on the long-term operation is that DS will need to be to be either replaced periodically or treated when OMBR-RO is operated continuously, which is the case for wastewater treatment applications. The determination of which is the best option is given by the economic analysis, which will be presented in the Chapter 4 of this Thesis.

Two removal mechanisms are integrated in OMBR: biological removal with physical removal by the FO membrane (ALTURKI, Abdulhakeem, MCDONALD, *et al.*, 2012b, LUO, Wenhai, PHAN, *et al.*, 2017). These mechanisms made the concentration of ACT, DIF and CBZ in the permeate of OMBR much lower than the equivalent found in the permeate of the MBR, which only relies on biological removal.

The advantage of the integration of biological and filtration mechanisms is that, since PhACs are biodegraded mainly by co-metabolism and following pseudo-first order kinetics under aerobic conditions (LAY, ZHANG, *et al.*, 2012, NSENGA KUMWIMBA, MENG, 2019), the high retention of PhAcs in the mixed liquor by the FO membrane and the consequent increase in its concentration ends up favoring biodegradation, which explains, for example, the high removal (94%) achieved in the OMBR for CBZ, a compound widely recognized as recalcitrant in conventional activated sludge treatment (DA SILVA, Jessica Rodrigues Pires, MONTEIRO, *et al.*, 2020, HAI, YANG, *et al.*, 2018). Removals above 90% for CBZ, DIF and ACT have also been reported in other

OMBRs (ALTURKI, Abdulhakeem, MCDONALD, *et al.*, 2012b, LUO, Wenhai, PHAN, *et al.*, 2017).

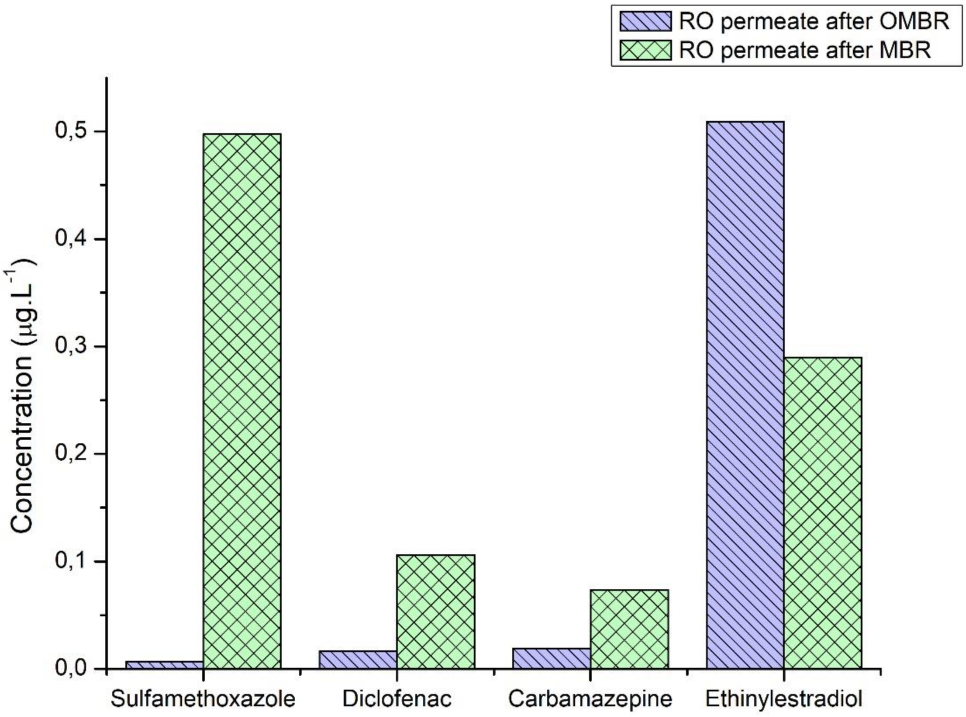
On the other hand, there was no relevant difference in the concentration of SMX in the permeate of OMBR and MBR, and the removal of EE2 was lower in the permeate of OMBR than in the permeate of MBR. These results point to a lesser biodegradation of these PhACs, with consequent accumulation in the mixed liquor that led to a greater permeation throught the FO membrane due to the increase in the concentration gradient. The biological removal mechanisms for PhAcs in engineering systems include mainly biodegradation and sorption (NSENGA KUMWIMBA, MENG, 2019). In the case of these two PhACs, both are relevant: EE2 and SMX spontaneously adsorb about 60.9% and 35.8%, respectively, in activated sludge biosolids, with SMX in particular having a strong affinity to adsorbe that results in a low desorption rate (HUANG, GUO, *et al.*, 2019), while biodegradation by co-metabolism has already been demonstrated for these two compounds (KASSOTAKI, BUTTIGLIERI, *et al.*, 2016, KATHIRVELU, SUBRAMANIAN, 2021). Considering that there was a low biomass growth, with a decrease in MLVSS (shown in Table 17) and there were no periodic sludge wastage, this may have reduced the mechanism of sorption removal in the sludge. In addition, studies show a relationship between increased salinity and inhibition of SMX removal (LIANG, ZHU, *et al.*, 2018) as well as relationship betwen increased stress and/or salinity with loss of the degradation capacities of bacterial strains present in activated sludge that degrade estrogens like EE2 (XIONG, YIN, *et al.*, 2020). Both factors may have contributed to the observed results of SMX and EE2 in the permeate of OMBR.

3.4.3 RO operation for draw solution recovery and production of reuse water

RO was operated to recover $K_4P_2O_7$ by concentrating DS, except in the case of seven DS that were analyzed directly by HPLC. $K_4P_2O_7$ was always recovered with a high efficiency (> 99% recovery measured by ionic conductivity) because of the charge and large size of the $K_4P_2O_7$ ions. Besides, in all experiments to recover $K_4P_2O_7$, RO permeate flux remained constant, even though no cleaning was performed in RO membrane. The constancy of the permeate flux after repeatedly using RO system indicates that there was no fouling in the membrane caused by any compounds that permeated through the FO membrane. This absence of fouling is attributed to an effective retention of foulants by FO, preventing them from permeating into the DS. The same observation was reported by Luo et al. (LUO, Wenhai, PHAN, *et al.*, 2017).

In terms of quality of RO permeate, Figure 21 and Table 18 show results obtained in RO permeate after OMBR and after MBR.

Figure 21: Pharmaceutically active compounds concentration in RO permeate after OMBR and MBR treatment.



*Acetaminophen was below method quantification limit (3 ng.L^{-1}) in all samples from OMBR-RO and from MBR-RO.

Table 18: Basic water quality parameters used to assess reuse water quality and their rejection (%) in RO permeate after OMBR and MBR treatment.

Parameter	**RO permeate after OMBR**	**Rejection***	**RO permeate after MBR**	**Rejection***
DOC (mg.L^{-1})	<0.5	>99%	<0.5	>99%
Color (Pt-Co)	<0,01	>99%	<0,01	>99%
Turbidity (NTU)	<0.9	>99%	<0.9	>99%

Nitrite (mg.L^{-1})	0.1	**	0.38	**
Nitrate (mg.L^{-1})	0.22	**	2.00	**
pH	6.0	**	6.0	**
Ortophosphate (PO_4^{3-}) (mg.L^{-1})	<0,5	>99%	<0,5	>99%

*Rejection was calculated considering the concentrations in the bioreactor feed and RO permeate.

**Not applicable

A very high (>99%) removal of DOC, color and turbidity were obtained in RO permeate, as expected due to the use of the RO membrane. Moreover, no nitrite nor nitrate were added to OMBR/MBR influent, so their presence in the RO permeate show that the two stages of nitrification (ammonium oxidation to nitrite, and nitrite oxidation to nitrate) occurred to some extent in OMBR and MBR bioreactors. This was expected due to the operating conditions employed e.g. high DO, SRT and HRT, that favor nitrification (METCALF, EDDY, 2003, PATHAK, PHUNTSHO, *et al.*, 2020). The result further shows that, despite the increase in conductivity in mixed liquor due to RSF in OMBR, nitrification still ocurred, which was also reported by Luo et al. (LUO, Wenhai, PHAN, *et al.*, 2017) when operating OMBR mixed liquor conducitivities up to 11mS/cm.

The presence of nitrite and nitrate in the permeate of the RO indicates that a portion of the nitrate permeated through the FO membrane and accumulated in the DS enough to permeate through the RO membrane, in the same way that happened with the PhACs. Nitrate in RO permeate after OMBR has also been reported by Qiu and Tin (QIU, TING, 2013). Orthophosphate was not observed in the permeate in either system, which was attributed to the large size of its hydrated complex as well and its charge, which allowed effective rejection by the FO and/or RO membrane. This result is in agreement with literature (LUO, Wenhai, PHAN, *et al.*, 2017).

Acetaminophen was below method quantification limit (3 ng.L^{-1}) in all samples both from OMBR-RO and MBR-RO. DIF, CBZ, SMX and EE2 were present in samples of both RO permeates, but in higher concentrations after MBR (74-500 ng.L^{-1}) than after OMBR (8-18 ng.L^{-1}). EE2 concentration, on the contrary, was in higher concentration in

RO permeate after OMBR (500 ng.L^{-1}) than after MBR (290 ng.L^{-1}). The presence of PhAcs in the RO permeate in different concentrations is due to the permeability of each solute through the RO membrane and to the concentration difference existing between the two sides of membrane, according to Equation 30. Permeability is directly related to physical-chemical properties of the membrane and the solute (shown in Tables 14 and 15, respectively). EE2, the compound present in the highest concentration in RO permeate, is also the most permeable (51.1 LMH) because it has a neutral charge in the operating pH (its pKa is 13.9) and this nullifies the electrostatic repulsion rejection mechanism by the RO membrane, leaving only the the mechanism of size exclusion. In addition, it is the most hydrophobic compound among the five analyzed, with log Kow of 3.67, which facilitates its affinity adsorption on the RO membrane, which is also hydrophobic, and consequently permeation to the RO permeate. The other PhACs are less hydrophobic than EE2 and, in the case of DIF and SMX, have charge, allowing greater rejections by the RO membrane and consequently much lower permeabilities than EE2 (SMX: 8.40 LMH; DIF: 0.91 LMH and CBZ 0.19 LMH).

3.4.4 Implications for the applicability of OMBR-RO in water reuse

The global water reuse market is rapidly expanding, especially for the applications that require high quality reuse water, which has resulted in intense research activity to advance wastewater treatment trains (BLANDIN, LE-CLECH, *et al.*, 2018, CAPODAGLIO, 2020). Recent progress has led to the emergence of OMBR as an alternative to the conventional MBR. However, it has not been fully demonstrated yet that technical improvements that may be obtained by OMBR-RO, when compared to MBR-RO, will be sufficient to support its application beyond laboratory scale (AB HAMID, SMART, *et al.*, 2020, BLANDIN, LE-CLECH, *et al.*, 2018). This Thesis sought to contribute to this discussion.

From the point of view of the water quality of reuse water, results obtained in this Thesis showed that both systems (MBR-RO and OMBR-RO) achieved highly effective removals of DOC and nutrients (shown in Table 18) and of ACT. OMBR-RO also achieved higher removals of SMX, DIF, CBZ, nitrate and nitrite than MBR-RO, but smaller removal of EE2 (as shown in Figure 21). The importance and necessity of achievieng such higher removals for these compounds depends on how the reuse water will be used, since each reuse option implies the attainment of specific water standards. For example, in water reuse for irrigation and potable reuse (either direct or indirect), PhACs removal is very important, and the results of this Thesis confirm an advantage of using OMBR to maximize the removal of some, though not all, PhACs. Besides, the greater removals of nitrite an nitrate achieved when using OMBR are not important when the goal is irrigation, since their presence in the water does not create any problem and can even be positive, but these greater removals are important for potable applications. On the other hand, there is no advantage in removing PhACs and nutrients when considering reuse in industrial applications, where their presence is not a problem, as they will not impact, directly or indirectly, living organisms. In this case, the main justifications for the replacement of MBR by OMBR are fouling alleviation in RO membrane and the introduction of double barrier of high retention membranes (FO and RO) that can provide a higher removal of small molecular size solutes both advantages demonstrated in this Thesis.

The effect of this double membrane barrier is illustrated by the concentrations of nitrate and nitrite in the RO permeate after OMBR, which were 10 and 4 times, respectively, smaller than in the counterpart MBR-RO (Table 18). A similar effect can be expected for other small molecular size solutes, as small solutes tend to permeate freely the MF or UF membranes of an MBR, but are partially retained by the FO membrane, thus increasing overall removal by the process. Moreover, the double barrier membrane can be useful to increase the resilience of the process, as the FO membrane serves as an extra barrier in case of operating problems that may temporarily decrease the removal of small solutes by RO. In the case of unforeseen disturbances, two high retention membranes instead of one reduce the likelihood of compounds appearing in the RO permeate.

Another relevant operational factor reported in this work is the maintenance of constant permeate flux during RO operation after OMBR, which means this operation would not require membrane cleaning. The main implication is the prolongation of the lifetime of the membranes due to less frequent chemical cleaning, which opens the possibility of reduced operating costs. In MBR-RO, on the other hand, fouling is recognized as a dominant problem which is heavily influenced by the MBR step ((FARIAS, HOWE, *et al.*, 2014, LUO, Wenhai, PHAN, *et al.*, 2017, WU, KITADE, *et al.*, 2013)) and thus chemical cleaning with relative frequency to recover the permeate flux is required.

Advantages in the process operation, greater resilience and an improvement in water quality considering removal of various PhACs can support OMBR-RO implementation, particularly when removal of PhACs is critical for the reuse option, and they are important factors to offset OMBR-RO drawbacks such as the energy expenditure needed to recover DS in the RO stage. This expendure is due to the the considerable osmotic pressure that is present in DS, even diluted, and must be overcome for the production of RO permeate. On the other hand, the relevant accumulation of solutes in DS, reported experimentally for the first time in this Thesis, represents an important issue to be considered in future research, due to the necessity of DS treatment, which becomes a drawback associated with this technology that can impact process feasibility.

3.5 Conclusions

Key aspects for the applicability of the combined process OMBR-RO for water reclamation were addressed in this Chapter.

The experimental results demonstrated that $K_4P_2O_7$ is a promising candidate as DS, as low solute permeability (0.05 LMH) and consequently a low reverse salt flux was obtained even when using FO membrane with less retention of salts than those usually used for FO applications, therefore confirming this Thesis Hypothesis. In despite of this result, there was still impact on acclimated biomass biological activity, not on biomass aerobic respiration but on biomass growth. Although this impact was observed, there were no negative effects on the process that could be linked to a reduction of biomass in the reactor, for example, there was no presence of organic carbon in the RO permeate, indicating accumulation in the process due to incomplete biodegradation because of reduced biomass. Another point of note was that the water flux decline in the FO membrane reached 58.5% due to both the reduction in the effective driving force (i.e. transmembrane osmotic pressure) for water transport and fouling.

Furthermore, it has been proven, for the first time in literature with experimental results, that PhACs diffuse and accumulate in the DS during continuous operation in non-negligible concentrations ($\mu g.L^{-1}$) after 72h of operation, which creates a demand for treatment of DS when it is continuously reconcentrated in a closed loop of OMBR-RO, in accordance with the Thesis Hypothesis. The feasibility of using UV/H_2O_2 to control this accumulation will be studied in Chapter 4.

The use of OMBR before RO allowed the maintenance of constant RO permeate flux and achievement of better water quality in terms of nitrite, nitrate, SMX, CBZ and DIF compared to MBR-RO, as these compounds were present in concentrations 4, 10, 74, 6 and 4 times lower, respectively, in the permeate of RO after OMBR when compared to the permeate of RO after MBR. These results are in accordance to the Thesis Hypothesis. However, water quality improvement was not observed for all the compounds, as expected, because EE2 concentration was double in RO permeate after OMBR compared to after MBR. This was attributed to a combination of two factors: 1) sludge’s loss of capacity to biodegrade EE2 due to increased salinity and low removal of EE2 by sorption in the sludge, leading to accumulation in the mixed liquor and consequent permeation at a considerable level for DS and ii) high permeability of EE2 through the RO membrane due to its physicochemical properties (neutral and very hydrophobic, so it has affinity with the hydrophobic RO membrane), making the barrier represented by the RO membrane not enough to reject all the EE2 that accumulated in DS. The only way to control the presence of EE2 in RO permeate is to degrade this compound while still in the DS that feeds the RO, avoiding the accumulation that creates the concentration gradient for the permeation to occur. This control is done by using the UV/H_2O_2 process to oxidate the compound, as will be discussed in Chapter 4.

Chapter 4 - Technical-economical analysis of osmotic versus conventional membrane bioreactors integrated with reverse osmosis and UV/hydrogen peroxide for water reuse

4.1 Introduction and objectives

In the last decade, many scientific efforts have been dedicated to understanding the fate of PhACs through existing and novel treatment process as well as their toxicity to many target organisms at different trophic levels (EJHED, FÅNG, *et al.*, 2018, KANAKARAJU, GLASS, *et al.*, 2018, OLIVEIRA, MURPHY, *et al.*, 2015, RADJENOVIĆ, PETROVIĆ, *et al.*, 2009, RODRIGUEZ-MOZAZ, RICART, *et al.*, 2015, SANTOS, ARAÚJO, *et al.*, 2010, THIEBAULT, BOUSSAFIR, *et al.*, 2017, VASQUEZ, LAMBRIANIDES, *et al.*, 2014, VULLIET, CREN-OLIVÉ, 2011). The results of these studies illustrated the low removal of many PhACs by biological treatment, as well as their potential ecotoxicity even at trace levels, which justify the concern with the topic of PhACs in water. Consequently, there is a tendency of including PhACs in new water quality regulations in the coming years, including those for water reuse (MIAROV, TAL, *et al.*, 2020, SILVA, Jessica Rodrigues Pires da, BORGES, *et al.*, 2020).

In light of these new restrictive environmental regulations that are under consideration, the water industry now is requiring strategies to improve the quality of final effluents in current and future treatment works, so that they can promote the sustainable and resilient management of wastewater works. An essential component of this strategy is technical-economical analysis of different available technologies. Technical analysis is necessary to ensure that a technology is feasible and preferably advantageous compared to other options, whereas economic analysis helps the comparability of technologies that are at different stages of progress e.g. promising technologies and commercially ready technologies. Thus, technical-economic analysis are a tool to analyze possible application/placement in the water market.

The most common treatment for advanced water reuse is biological treatment followed by microfiltration and reverse osmosis (CAPODAGLIO, 2020, HOLLOWAY, MILLER-ROBBIE, *et al.*, 2016, PIRAS, SANTORO, *et al.*, 2020) This treatment train has been the subject of technical-economic analyzes that have demonstrated its feasibility, including for the removal of micropollutants(FONSECA, Meliza Jennifer da Costa, SILVA, *et al.*, 2021, GOSWAMI, VINOTH KUMAR, *et al.*, 2018, WANG, Siyu, LIU, *et al.*, 2019). It can therefore be considered a baseline scenario using commercially ready technologies, which can be compared to other promising but not yet commercial options.

FO-based processes integrated with reverse osmosis have been proposed as innovative alternatives for wastewater treatment and reuse. For example, anaerobic OMBR integrated with RO (AB HAMID, SMART, *et al.*, 2020, VINARDELL, ASTALS, *et al.*, 2020), forward osmosis with RO (VALLADARES LINARES, LI, *et al.*, 2016) and ultrafiltration OMBR with reverse osmosis (HOLLOWAY, MILLER-ROBBIE, *et al.*, 2016) have been subject to technical-economical analysis. The results of these works indicate the feasibility and sustainability of FO-based processes, however, they have not been fully demonstrated yet (AB HAMID, SMART, *et al.*, 2020) because of the large number of variables and possible arrangements of FO-based processes that still need to be explored. In this work, aerobic OMBR integrated with RO for clean water production and reconcentration of DS, which is then recirculated in a closed-loop to OMBR, was the arrangement evaluated and compared with the consolidated MBR-RO. The replacement of the conventional MBR by an OMBR brings advantages suuch as the reduction of fouling and scaling potential on the RO, because of FO retention of most soluble microbial products; the elimination of the need of disposing of RO retentate, as it is the draw solution that is continously recirculated; and the improvement of reclaimed water quality because of the the presence of a double layer of non-porous membrane membranes. These advantages have been cited in the literature (BLANDIN, LE-CLECH, *et al.*, 2018, CORZO, DE LA TORRE, *et al.*, 2017, ZHANG, Bangxi, SONG, *et al.*, 2017) and confirmed with the results of this Thesis as discussed in Chapter 3.

However, a disadvantage of this arrangement is solute accumulation in the DS (D'HAESE, LE-CLECH, *et al.*, 2013, PHUNTSHO, KIM, *et al.*, 2017), which has been further demonstrated in this Thesis (section 3.4.2). This accumulation might negatively impact the quality of RO permeate (i.e. reclaimed water) and is therefore imperative to investigate ways of controlling it, which can be done either by replacing or treating the DS; an economic analysis indicates the most favorable option. Due to the nature of the DS (e.g. saline and with a very low concentration of organics and nutrients), in case DS treatment is the choice, only a chemical oxidation treatment would be suitable for treatment to control the solute accumulation. Advanced Oxidation Processes (AOPs) stand out for the generation of strong and non-specific oxidants (OH-radicals), and UV-based AOPs have received considerable attention in the past decade for PhACs removal from wastewater (KANAKARAJU, GLASS, *et al.*, 2018, OTURAN, AARON, 2014, YANG, ZHOU, *et al.*, 2014). For these reasons, UV/H_2O_2 was chosen among the AOPs as the alternative for assessing the treatment of DS. Since the effect of salinity on UV-based processes is not well-defined, and a light absorption or scattering effect from dissolved organic and inorganic compound could affect the process (MORENO-ANDRÉS, ROMERO-MARTÍNEZ, *et al.*, 2017), technical analysis of the UV/H_2O_2 to treat DS, which has high salinity, was necessary prior to the economical analysis.

Thus, the objectives of this Chapter were:

- To evaluate the technical feasibility of using UV/H_2O_2 to treat DS (corresponding to parts of specific objective 5);

- To verify which is the best option in economic terms to address the issue of PhACs accumulation in DS;

- To make a preliminary estimate of the capital cost expenditures (CAPEX) and operating expenses (OPEX) for OMBR-RO with UV/H_2O_2 to treat the DS and for MBR-RO with UV/H_2O_2 to treat RO retentate, comparing these costs (corresponding to parts of specific objective 6);

- To use Net Present Value (NPV) to calculate the minimum cost of reclaimed water that is economically feasible for MBR-RO and OMBR-RO (corresponding to parts of specific objective 6).

4.2 Materials and Methods

4.2.1 Technical Analysis

Experimental setup

The same experimental UV system described in section 2.3.5, was used.

Experimental protocol

Two solutions of 8.0L each were prepared by dissolving the same amount of a standard solution contaning PhACs in MiliQ water, the only difference being that in one of them 33.5g.L^{-1} of $K_4P_2O_7$ were also added (corresponding to a conductivity of 25 mS.cm^{-1}, simulating a concentrated DS). MiliQ water was used to ensure that $K_4P_2O_7$ was the only additional solute in the matrix other than the PhACs, and therefore any changes in degradation between the solutions could be unequivocally attributed to the $K_4P_2O_7$ and not other matrix effects. PhACs concentration in the solution was in the range of 1-7 µg.L^{-1}. These concentrations were chosen to reflect those found in diluted DS (in accordance with section 3.4.2). Furthermore, they are sufficiently low to prevent interactions between PhACs and their transformation products as well as to assure degradation is independant of initial concentration, thereby allowing considering a pseudo-first order kinetics (SHU, BOLTON, *et al.*, 2013, WOLS, HOFMAN-CARIS, *et al.*, 2013).

Five experiments were carried out with each solution (with and without $K_4P_2O_7$). Experiments were designed to be carried out under identical operating conditions, so that the only difference was the presence of the $K_4P_2O_7$. In each experiment, a constant dose of H_2O_2 (30 mg.L^{-1}) was used under different irradiation times (5, 10, 20, 40 and 60min, corresponding to UV doses of 204, 408, 816, 1630 and 2448 mJ.cm^{-2}, respectively). Three replicates were made for the UV dose of 204 mJ.cm^{-2} to verify the experimental error. The UV and H_2O_2 doses were established according to previous results in the literature (WOLS, HOFMAN-CARIS, *et al.*, 2013). Sodium bisulfite was added at the end of each experiment to quench the reaction. A sample was collected at the end of each experiment, and these samples as well as a sample from the original (feed) solution were analyzed by SPE-HPLC for PhAC quantification.

4.2.2 Economic Analysis

Methodology of economic evaluation

This section presents an economic analysis based on computing CAPEX and OPEX costs over a 20-year period of investment, as usual for wastewater recovery projects (HOLLOWAY, MILLER-ROBBIE, *et al.*, 2016, VALLADARES LINARES, LI, *et al.*, 2016). NPV was calculated by Equation 31:

Equation 31

$$NPV = \sum_{t=0}^{t=20} \frac{R_t}{(1+i)^t}$$

Where Rt = net cash inflow – outflows during a single period t.

i = interest rate (Interest rate of 5.68% per year was considered, which was the world average between 2020 and 2019[10])

t = numer of time periods

In year 0, before the startup of the facility, Rt is given by the CAPEX invested to construct the facility and during the operation time (years 1 to 20), Rt is given by Equation 32:

Equation 32

$$R_t = Revenue - OPEX$$

Minimum revenue was calculated by an iterative process and corresponds to the value that zeroed the project's NPV in 20 years. Since the project is profitable when NPV is above zero, any revenue above the minimum will make the project profitable thus feasible from an economic point of view (the higher the revenue, the more profitable). The revenue was then divided by the plant´s capacity of water production to reach the reclaimed water price per m³ of treated water.

A sensitivy analysis was made taking into consideration the following parameters: FO membrane permeability, membrane cost and DS osmotic pressure. A calculation spreadsheet was generated considering the methodology and the cost assumptions presented in item 2.2.3.

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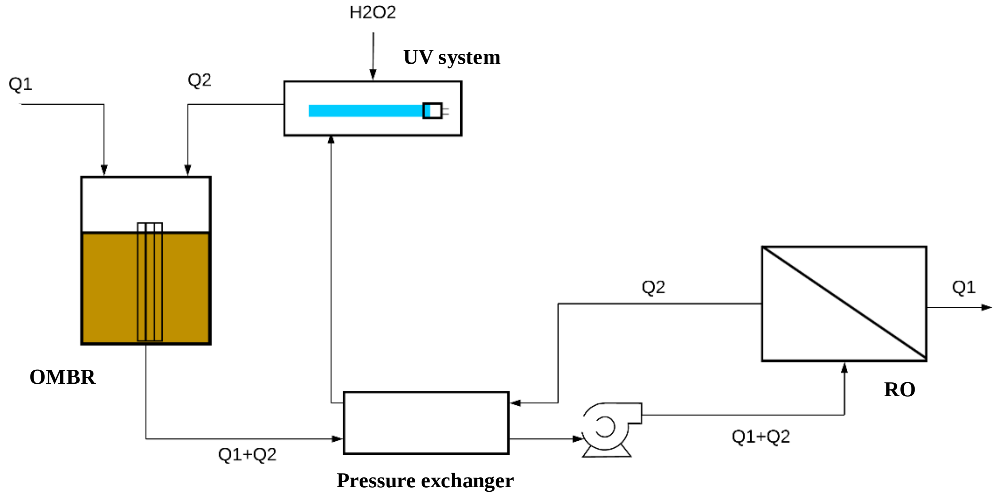
[10] Source: https://tradingeconomics.com/country-list/interest-rate, accessed November 9th,2020.

Technologies analyzed

Two technologies trains were compared in terms of costs for wastewater treatment and reuse. The description of these tecnologies for a full-scale operation is given below. In both cases, feed water was considered the same, with characteristics of high biodegradability and osmotic pressure of approximately 0.3 bar.

OMBR-RO with AOP - Figure 22 shows a schematic diagram of this process.

Figure 22: Schematic diagram of OMBR-RO with UV/H_2O_2 in a full-scale plant.

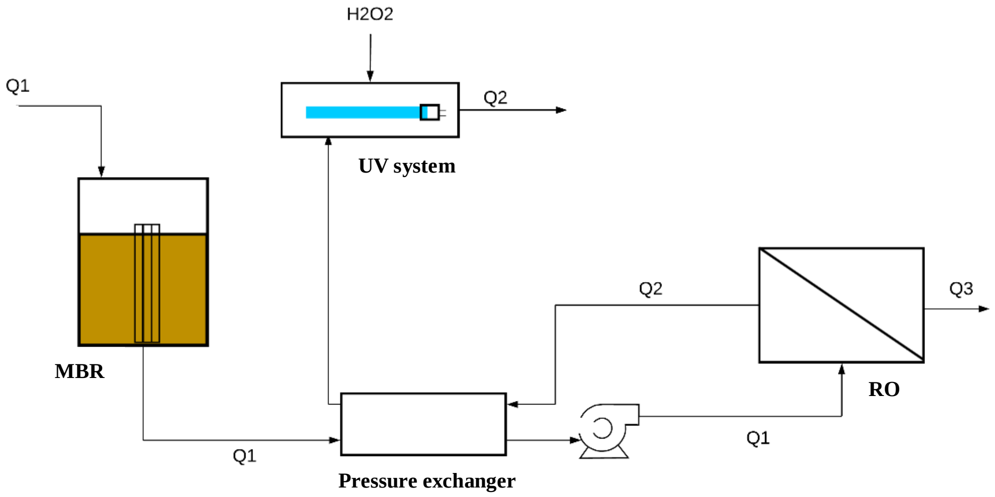


Concentrated DS (Q2) is diluted by the extraction of water from the mixed liquor through the FO membrane, Q1, which corresponds to the flow of influent wastewater. Q2 is considered to be a solution of $K_4P_2O_7$ with osmotic pressure of 11 bar (in sensitivity analysis osmotic pressures ranging from 9 to 25 bar were also assessed). Q1+Q2, corresponding to the diluted DS, is fed to the RO for recover. RO permeate is the reuse water and corresponds to Q1.

UV/H_2O_2 is triggered whenever the accumulation of PhACs in DS is considered high enough, which according to experimental results of Chapter 3 is around every 72h. It is noted that a pressure exchanger was included to maximize energy efficiency, since Q2 at the RO outlet is under high pressure due to having been pressurized at the RO inlet, but it is not desired to have this high pressure at the inlet of the OMBR. On the other hand, the output of OMBR has low hydraulic pressure, which will need to be increased for RO.

MBR-RO with AOP – Figure 23 shows a schematic diagram of this process.

Figure 23: Schematic diagram of MBR-RO with UV/H_2O_2 in a full-scale plant.



MBR permeate (Q1), which corresponds to the flow of influent water, feeds the RO. The pressure exchanger was placed to maximize energy efficiency, in a similar way to OMBR-RO. RO permeate (Q3) corresponds to reclaimed water produced by the MBR-RO. In this system, not all MBR permeate (Q1) is converted into reclaimed water in the RO (Q3), since the recovery of the RO is 75% but the retentate (Q2) is not recirculated, but rather treated by UV/H_2O_2 to reduce its concentration of organics and then discharged (low quality reuse may also be possible).

OPEX and CAPEX calculations

The calculations in this section were based on the following assumptions:

- The comparison between MBR-RO and OMBR-RO is based on a production capacity of 24,000 $m^3.d^{-1}$ for both systems;

- The cost for FO membrane is USD 56 per m² (VALLADARES LINARES, LI, et al., 2016) (in sensitivity analysis prices of USD 20 to 70 per m² were also assessed) and the cost for RO membrane is USD 15 per m²[11].

- Energy consumption by reverse osmosis was calculated by pump power for the pumps shown in Figures 22 and 23. Pump power was calculated by Equation 34:

Equation 33

$$Power = \frac{\Delta P \, . Q}{\eta}$$

Where ΔP = pressure difference between discharge and suction of the pump (at the intlet of RO pressure was set at 30 bar)

Q = volumetric flow

η = pump efficiency (75%)

- For calculations of electric energy consumption of the pumps, the use of a pressure exchanger was considered, positioned according to Figures 22 and 23. Pressure exchanger efficiency was set at 95% of energy recovery from the current exiting the RO (RO retentate).

- FO water permeability was 0.6 $L.m^{-1}.h^{-1}.bar^{-1}$ ($LMH.bar^{-1}$) (in sensitivity analysis water permeabilities ranging from 0.15 to 2.5 $L.m^{-1}.h^{-1}.bar^{-1}$ were also assessed) and RO water permeability for both treatment trains was 1.5 $L.m^{-1}.h^{-1}.bar^{-1}$;

- RO water recovery was set at 50% in the OMBR-RO system and 75% in the MBR-RO system.

- The conductivity of the mixed liquor is set at 10 $mS.cm^{-1}$, which corresponds to an osmotic pressure on the side of the mixed liquor of approximately 3.50 bar;

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[11] This cost was informed by vendors of commercial RO modules.

- Energy consumption by MBR was 0.50 kWh per cubic meter of water treated and other operating costs, including chemical cleaning, are USD 0.046 per cubic meter of water treated ((XIAO, LIANG, et al., 2019).

- For UV/ H_2O_2 calculations, OPEX are the cost of H_2O_2 and electrical energy, given by EE/O (using Equation 20). For UV/ H_2O_2 used in DS, doses necessary to obtain 99% removal of EE2 (H_2O_2 30 $mg.L^{-1}$ and 816 $mJ.cm^{-2}$) were considered, since EE2 is the most critical PhAC in DS (as discussed in section 3.4.3). For UV/H_2O_2 used in the RO retentate, the conditions necessary to obtain the mineralization of biologically treated effluent (H_2O_2 200 $mg.L^{-1}$ and 1305600 $mJ.cm^{-2}$, as given in section 2.4.4) were considered;

- It was considered that the UV/H_2O_2 system used in the DS would be activated every 72 hours, because after this time interval of continuous operation there was already an accumulation of PhACs at $\mu g.L^{-1}$ levels in DS (as discussed in section 3.4.2);

- Electrical energy costs were set to 0.12 USD. kWh^{-1} (this is the value for electricity for industries in São Paulo city as of 2020[12]);

- Membrane lifetime was considered 5 years for FO membranes and for RO membranes after MBR and 10 years for RO membranes after OMBR. The longer lifetime after OMBR was due to the lack (or very reduced rate) of membrane cleaning in RO after OMBR (this assumption is valid considering the results discussed in section 3.4.3);

- Depreciation (considering all equipment, except membrane replacement, which is accounted separetely due to lifetime) was set at 20 years;

---

[12] Assuming a exchange rate of 1USD to 5.3R$.

- Maintenance and labor were considered 15% of OPEX costs (VALLADARES LINARES, LI, et al., 2016);

- Chemical cleaning was considered for FO membranes and RO membranes after MBR (no chemical cleaning in RO after OMBR). Considering the absence of defined cleaning protocols for FO membranes, the RO membrane cleaning protocol given by the manufacturer (Dow-DuPont) was preliminarily adopted for both RO and FO. A cleaning cycle consists of complete immersion of the membrane module in solutions of 0.2% NaOH (USD 300/ton), 1% Na_4EDTA (USD 1420/ton), 0.025% NaDSS (USD 1200/ton), 0.2% HCl (USD 210/ton) and 1% $Na_2S_2O_4$ (USD 900/ton), which is sufficient to remove all types of fouling (inorganic salts, sulfate scales, metal oxides, silt, silica, biofilms and organics). Six cleaning cycles per year were considered, and the volume of the modules considered was: 7.8L per RO module (each module with 7.2 m²) and 29L per FO module (each module with 27 m²). Costs for chemicals are based on vendor quotes.

Table 19 presents the detailed CAPEX cost for OMBR and RO systems, with materials, engineering, procurement and constructions costs calculated based on membrane costs, following a methodology usually adopted for preliminary economic analysis (OSIPI, SECCHI, et al., 2018, VALLADARES LINARES, LI, et al., 2016). For MBR system, CAPEX costs were calculated as a function of volume of treated water, considering USD 600 per cubic meter of water treated, which includes pretreatment to the MBR (XIAO, LIANG, et al., 2019) whereas for UV systems, CAPEX was based on previously reported data (FONSECA, Meliza Jennifer da Costa, SILVA, *et al.*, 2021).

Table 19: CAPEX costs for OMBR and RO systems.

Components	**FO system (VALLADARES LINARES, LI, et al., 2016)**	**Low-pressure RO system (OSIPI, SECCHI, et al., 2018)**

Membranes	29.4%	5.5%
Equipment and materials related to membranes, incluing pressure vessels)	22.5% (no pressure vessels)	26.5%
Pressure exchangers and pumps	6.6 % (no pressure exchangers)	22%
Others (Pretreatment, civil engineering, design, legal services, installation and intakes/outfalls)	41,5%	46%

2.2.4 Methodology to choose the best option for DS destination

To analyze which is the best option for destination of DS, DS replacement or treatment by UV/H_2O_2, the following assumptions were made:

- The treatment or replacement of the DS must be carried out every 72h;

- $K_4P_2O_7$ cost was set at USD 3500/ton and H_2O_2 cost was set at USD 600/ton (costs for chemicals are based on vendor quotes);

- Concentration of $K_4P_2O_7$ is 18g.L^{-1}, which corresponds to an osmotic pressure of approximately 11 bar;

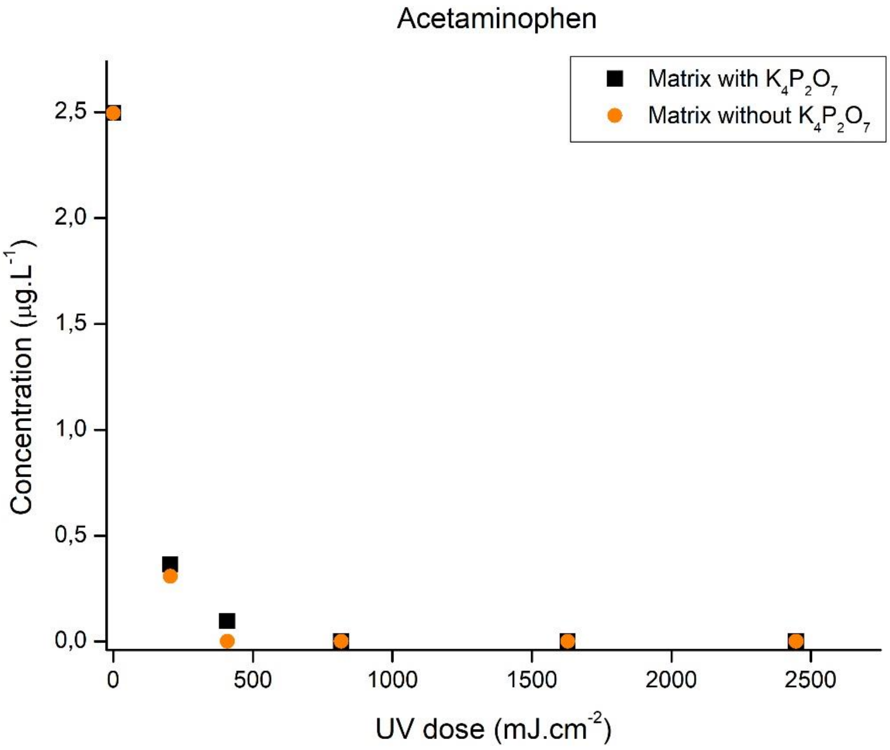
- Electricity consumption in the UV/H_2O_2 treatment was calculated in the same way as mentioned in the item above for EE2.

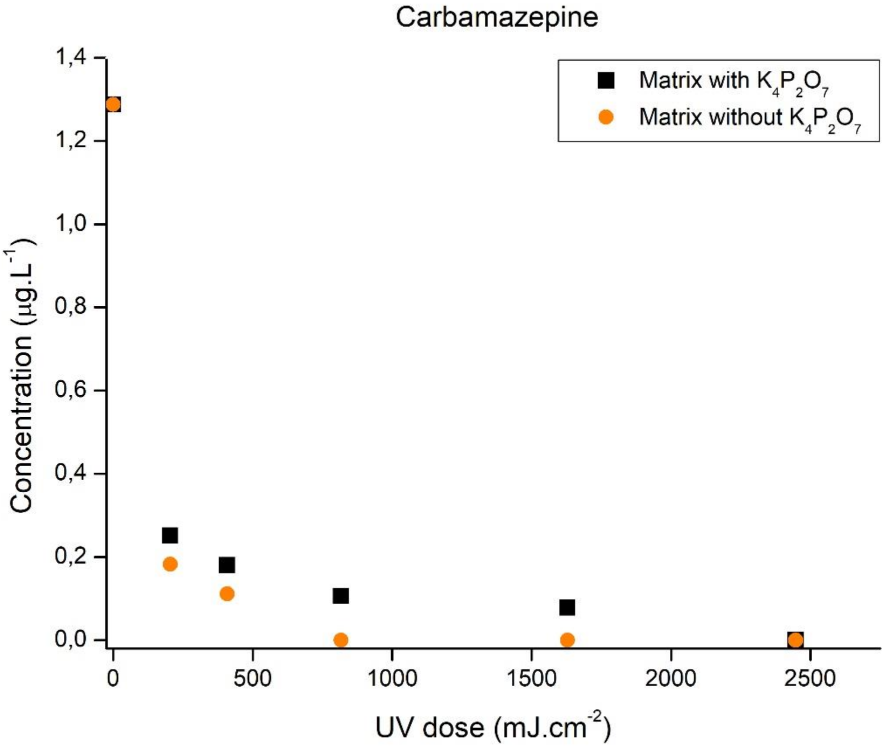
4.3 Results and Discussion

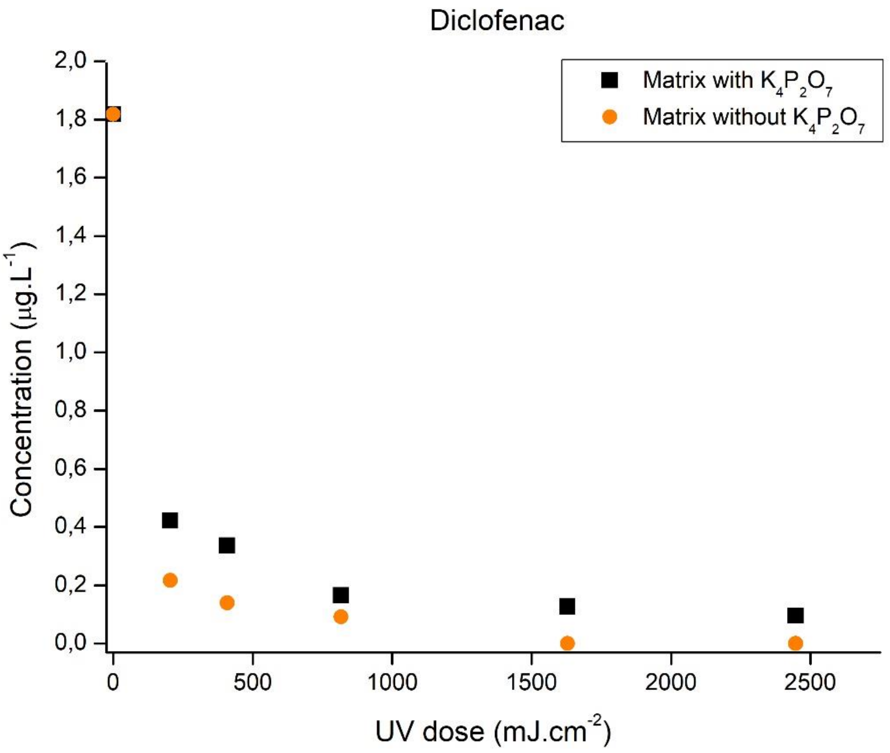
4.3.1 Technical Analysis

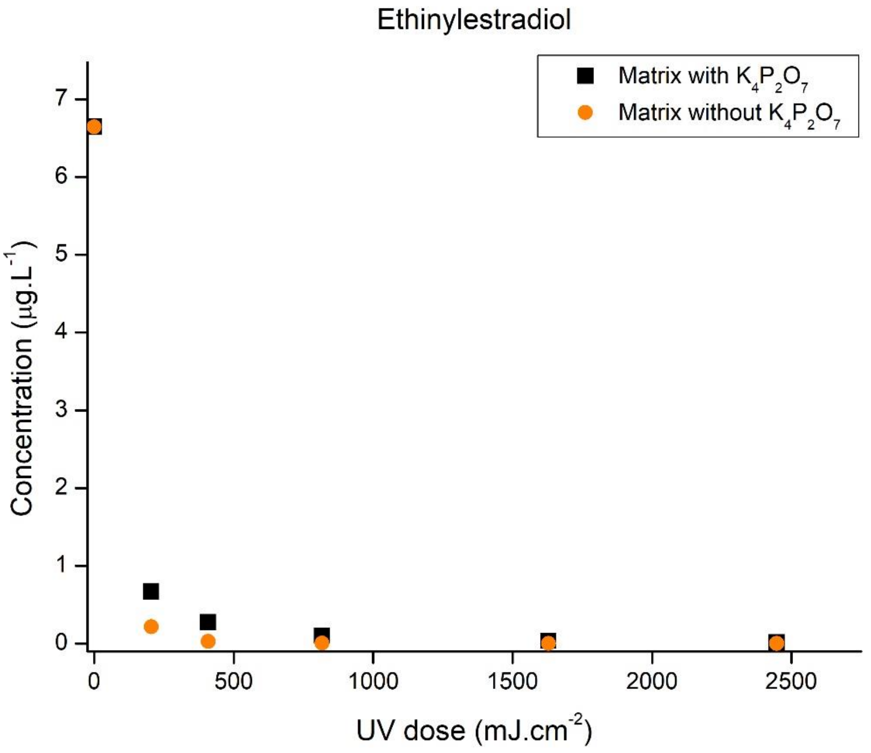
The results of the degradation of each of the five PhACs in the two aqueous matrices (with and without $K_4P_2O_7$) are presented in Figure 24.

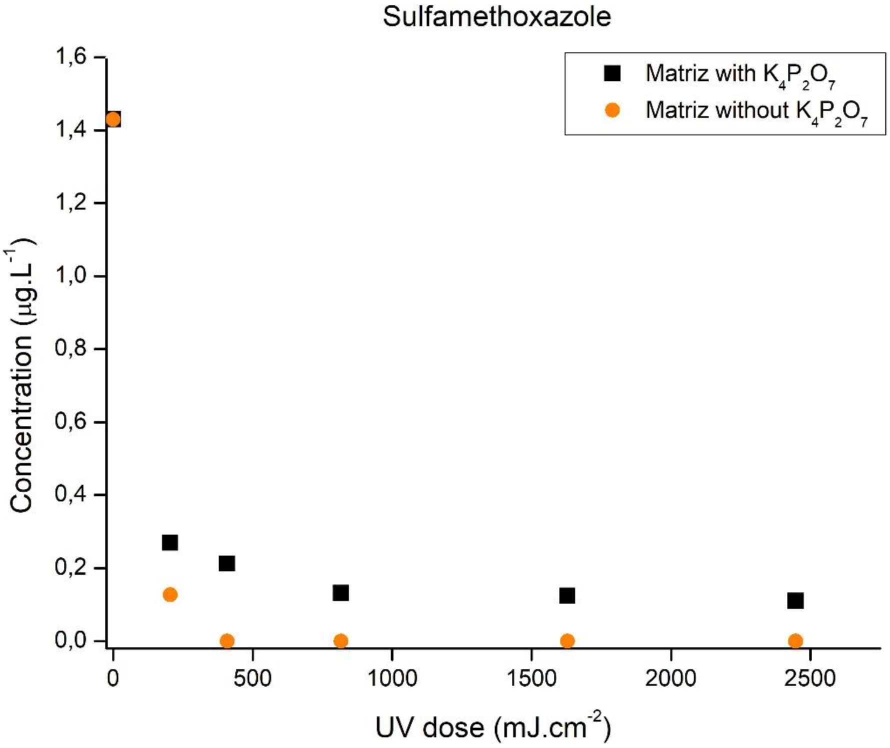
Figure 24: Concentration of PhACs in the solution depending on the matrix (with and without potassium pyrophosphate) and the UV dose.






Diclofenac
■ Matrix with $K_4P_2O_7$
● Matrix without $K_4P_2O_7$
Concentration (µg.L^{-1})
2,0
1,8
1,6
1,4
1,2
1,0
0,8
0,6
0,4
0,2
0,0
0
500
1000
1500
2000
2500
UV dose (mJ.cm^{-2})


Ethinylestradiol
■ Matrix with $K_4P_2O_7$
● Matrix without $K_4P_2O_7$
Concentration (µg.L^{-1})
7
6
5
4
3
2
1
0
0
500
1000
1500
2000
2500
UV dose (mJ.cm^{-2})



*Removals were calculated based on feed concentration.
** H_2O_2 dose was 30 mg.L^{-1} for all UV doses.
**Standard deviation for a UV dose of 204 mJ.cm^{-2} was: ACT ±0.036, SMX ± 0.010, DIF ±0.016, CBZ ±0.012 and EE2 ± 0.010.

It is observed that for all PhACS there was a difference in the remaining concentration after an UV dose depending on the matrix. The remaining concentration in the solution was always higher in the matrix with $K_4P_2O_7$ than in the matrix without $K_4P_2O_7$, for the same irradiation time and H_2O_2 dose. Although this behavior has been observed for all PhACs, it was much less pronounced in ACT and EE2, and much more notable for DIF, SMX and CBZ. These results allow a conclusion that, for the same H_2O_2 and UV doses and the same initial concentration of PhACs, $K_4P_2O_7$ reduced, though not inhibited, the degradation of all the PhACs in the solution, although the extent of reduction was different depending on the compound.

The matrix heavily influences the dynamics of an AOP; it is known, for example, that several organic constituents and inorganisms found in aqueous matrices act as hydroxyl scavengers, decreasing the oxidation efficiency due to the competition with the target solutes for the hydroxyl radicals, effectively consuming these radicals(MIKLOS, REMY, *et al.*, 2018, RIBEIRO, MOREIRA, *et al.*, 2019). In the experiments in this section, miliQ water matrix was used, thus, the only components of the matrix were $K_4P_2O_7$ and PhACs. Therefore, the difference in degradation can be attributed to the presence of pyrophosphate anions.

Phosphates in general are not usually mentioned as scavengers in AOP: carbonates, chloride, nitrate and organic substances such as humic and fulvic acids, expressed as DOC, are considered classic scavengers (PARSONS, 2004). However, recent studies have shown that in phosphate has hydroxyl scavenger power, since the hydroxyl reacts with the phosphate removing it from the reaction mixture, although at a much lower rate than the hydroxyl reaction with almost all organic compounds. This is why the role of phosphates as scavengers is rarely mentioned (CHEN, 2019, KHOSRAVIFARSANI, SHABESTANI-MONFARED, *et al.*, 2016). Although there are no studies testing the scavenger power of $K_4P_2O_7$ specifically, which is the simplest of polyphosphates, the results of the present study indicate that this scavenger power also exists with $K_4P_2O_7$. Therefore, in the presence of $K_4P_2O_7$, there would be less availability of the hydroxyl radical, leading to lower degradation rates in this solution. To compensate for this apparent scavenger effect of pyrophosphate anions, higher doses of UV irradiation will be needed to generate more hydroxyl radicals, and it can be expected that these irradiation doses will need to be increasingly larger as the concentration of $K_4P_2O_7$ in the solution increases, which is a factor that favors the operation of OMBR using DS with low $K_4P_2O_7$ concentrations.

In the case of EE2, CBZ and ACT, a longer UV dose (1630, 2448 and 816 $mJ.cm^{-2}$, respectively) was enough to bring the concentrations below MQL in the $K_4P_2O_7$ matrix (removals>99.9%) with H_2O_2 dose 30 $mg.L^{-1}$. In the case of DIF and SMX, even with 2440 $mJ.cm^{-1}$, final concentration was not below MQL, although high removals have been achieved (95 and 92%, respectively). It is noted that full-scale processes do not operate with high irradiation times (RODRÍGUEZ-CHUECA, LASKI, *et al.*, 2018) due to the large volumetric flow of effluent involved and the high operational cost that this would entail. Considering a more likely scenario of UV dose of 204 $mJ.cm^{-2}$ with H_2O_2 dose of 30 $mg.L^{-1}$, it would be possible to obtain removals of ACT, SMX, DIF, CBZ and EE2 of 85%, 81%, 77%, 81% and 90%, respectively, in the matrix with the presence of $K_4P_2O_7$, which signals the feasibility of this process for controlling the PhACs in the DS.

4.3.2 Economic Analysis

Choice between DS treatment and disposal

Two options were considered for the control of PhACs permeating throught the FO membrane from the mixed liquor: DS periodic replacement or DS treatment by UV/H_2O_2, since the latter was proven to be possible in the section above. Economic analysis dictates which alternative is more financially favorable. The costs involved in each option are shown in Table 20.

Table 20: Costs for the alternatives DS replacement and DS treatment

Alternatives/Costs	DS replacement Cost	DS treatment
CAPEX	-	USD 1,619,524.00
CAPEX (per treated m^3)	-	USD 0.01
OPEX (per treated m^3)	USD 0.18*	USD 0.11 per 1000m^3 treated

*excluding the expenses to manage the streams containing PhACs residues (only accounts for expenses with the acquisition of $K_4P_2O_7$).

**CAPEX and OPEX costs fo treatment refer only to UV/H_2O_2 treatment in DS.

Results show the relevant economic advantage of treating DS with UV/H_2O_2, even considering the cost of acquisition of UV systems dimensioned to treat a high flow rate (Q2), but whose activation only occurs every 72 hours. In other words, even when computing the cost of acquiring equipment that is inoperable for large periods of time, the cost is still lower because the operating cost for treating the DS is low.

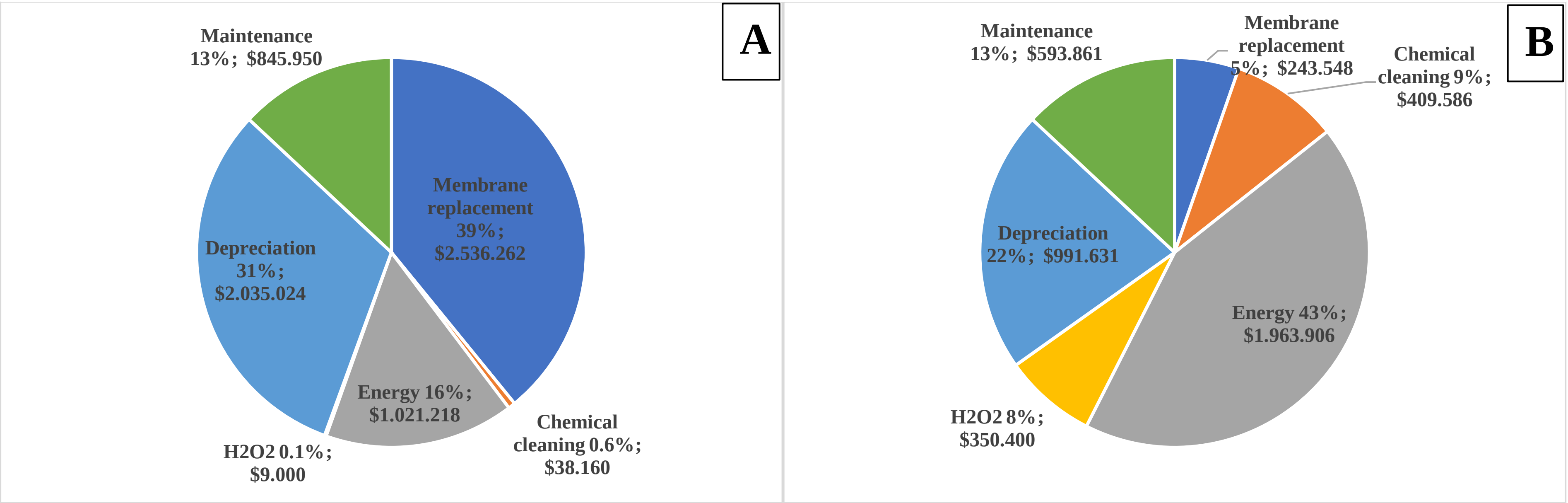
OPEX and CAPEX

Tables 21 CAPEX costs for each technology involved, and Figure 25 illustrates OPEX costs on an annual basis.

Table 21: CAPEX costs for the systems.

	OMBR		**RO (after OMBR)**		**RO (after MBR)**		**MBR (including pretreament)**	**UV (in MBR-RO)**	**UV (in OMBR-RO)**
	% of Total Cost	Cost (USD)	% of Total Cost	Cost (USD)	% of Total Cost	Cost (USD)	Cost (USD)	Cost (USD)	Cost (USD)
Membranes	29.4	12,411,348	6	539,922	5.5	353,742	864,000	-	-
Equipment and materials	22.5	9,498,480	25	2,454,190	25	1,607,918	-	-	-
Pressure vessels	-	-	1.5	147,251	1.5	96,475	-	-	-
Pressure exchangers	-	-	2.2	215,969	2.2	141,497	-	-	-
Pumps	6.5	2,744,005	20	1,943,719	19.8	1,273,471	-	-	-
Other construction costs	41.6	17,561,635	46	4,515,710	46	2,958,568	-	-	-
Other costs	-	-	-	-	-	-	13,536,000	404,881	1,619,524
CAPEX (USD)	**42,215,468**		**9,816,760**		**6,431,671**		**14,400,000**	**404,881**	**1,619,524**

Figure 25: Annual OPEX costs for A) OMBR-RO system with UV/H_2O_2 for DS treatment and B) MBR-RO system with UV/ H_2O_2 for treatment of RO retentate.



For CAPEX, a major cost is cost of the FO membrane, well above the cost of the RO membrane (Table 21). This difference is due to i) higher cost per m² of membrane (USD 56 in FO, USD15 in RO), which can be attributed to the higher production cost for a newly developed membrane for FO compared to the production of commercial RO membranes, that have been on the market for years and ii) a relatively low permeability (0.60 $Lm^{-1}.h^{-1}.bar^{-1}$), low DS osmotic pressure on DS side and mixed liquor osmotic pressure of 3.50 bar, due to salinity build-up. As a result, water flux is relatively low, which leads to a large area of membrane required in the FO.

The RO process after OMBR also has a higher price due to the lower permeate flux achieved in this process compared to RO after MBR, for the same applied pressure (30 bar). This lower flux is due to the existence of the osmotic pressure in the diluted DS, which must be exceeded for permeate production, while MBR permeate has negligible osmotic pressure thus achieving higher water flux for the same applied pressure.

Finally, the cost of the UV system associated with OMBR-RO is higher because the flow rate treated by this process (Q2 in Figure 22) corresponds to a flow rate greater than that treated by UV in the MBR-RO process (Q2 in Figure 23). As a result of these higher costs, CAPEX of the OMBR-RO with UV/H_2O_2 is 2.5 times greater than that of the MBR-RO system (Figure 26).

Figure 26: CAPEX and OPEX costs and minimum water cost of water production per m³ produced.

*Minimum water cost calculated based on plant water capacity of 24,000 m³.day^{-1} and zero NPV throughout the 20-year lifetime of the project for a interest rate of 5.68% per year.

In terms of OPEX, it can be seen in Figure 25 that in the OMBR-RO system with UV/H_2O_2 there is reduction in costs related to chemical cleaning, due to the absence of cleaning of the RO membranes, and consumption of H_2O_2, since the UV/H_2O_2 treatment occurs intermittently and at concentration of 30 mg.L^{-1}, whereas in MBR-RO it is continuous and at a high concentration of 200 mg.L^{-1}. Energy expenditure in the RO stage of both processes was very similar (USD 0.12 per treated m³ in RO after OMBR versus USD 0.13 per treated m³ in RO after MBR), confirming that FO-based processes such as OMBR are not particularly energetically favorable when compared to MBR-RO due to the need for recovery of DS that is at a higher flow rate at the inlet of RO (Q1 + Q2 in Figure 22) than its counterpart in MBR-RO (Q1 in Figure 23), thus requiring high pumper power according to Equation 34. This result is corroborated in the review paper by SHAFFER, WERBER, et al., 2015. On the other hand, the energy expenditure with UV/H_2O_2 in the MBR-RO system was much higher (USD 0.03 per treated m³ versus

USD 0.0004 per treated m³ in OMBR-RO) since the UV system in the MBR-RO not only operated continuously, but also with a high UV dose (1305600 mJ.cm^{-2}), necessary to obtain high DOC removal, as shown in the results of Chapter 2. Consequently, the total energy costs considering the complete systems were lower in the OMBR-RO-UV/H_2O_2.

In despite of lower energy costs, the total OPEX cost of OMBR-RO-UV/H_2O_2 was still 42% higher than the MBR-RO-UV/H_2O_2 (Figure 26) due to depreciation and membrane replacement costs, which together accounted for 58% of OPEX as shown in Figue 25. These costs are directly linked to the CAPEX cost. As the CAPEX of OMBR-RO-UV/H_2O_2 is 2.5 times higher than that of MBR-RO-UV/H_2O_2, this ended up impacting OPEX as well. Therefore, the reduction in CAPEX is crucial to reduce the overall cost of a OMBR-RO-UV/H_2O_2 project.

3.4 Minimum cost of reclaimed water

After obtaining the CAPEX and OPEX costs of the treatment scenarios, the minimum cost per m³ of produced water was calculated based on a plant capacity of 24,000 m³.day^{-1} and a revenue that zeroes the NPV. The minimum cost of water production was given in Figure 26. The cost of OMBR-RO-UV/H_2O_2 is 73% higher than the cost of the proposed MBR-RO-UV/H_2O_2 technology due to the higher CAPEX and OPEX costs discussed in the item above.

It is noteworthy that in the case of MBR-RO-UV/H_2O_2, besides the annual production of 24,000 m³.day^{-1} of high quality reused water, there is also the generation of 7,993 m³.day^{-1} corresponding to RO retentate, that underwent UV treatment dose of 130.56 kJ.m^{-2} and H_2O_2 dose of 200 mg.L^{-1} for oxidation of organic matter. Considering that this dose obtained mineralization of biologically treated effluent (section 2.4.4), it can be considered that the application of these doses in the RO retentate whose feed was biologically treated effluent would obtain levels of organic matter removal sufficient at least for disposal (in Brazil, for example, the legislation for the disposal of effluents requires a minimum removal of 60% of organic matter measured as BOD_5 (BRASIL, 2011)). UV/H_2O_2 was considered only to allow the disposal in compliance with legislation; however, it is possible to consider this RO retentate as a reuse water of inferior quality, which could generate some additional revenue for the project in addition to the production of 24,000 m³.day^{-1} of high quality water.

The minimum costs of water production by OMBR-RO-UV/H_2O_2 can be compared with the average cost of residential water currently practiced to assess immediate feasibility, that is, if OMBR-RO technology were commercialized at the present without actions to reduce costs. Water prices in the USA are between USD 1.56 - 1.64 per m³ consumed as of 2018 (most recent date available)[13], depending on monthly consumption, where the higher the consumption, the more expensive. In Brazil, the average cost of residential water in the State of São Paulo in 2020 is between USD 0.8-2.20 per m³ consumed, depending on monthly consumption[14]. Therefore, the minimum water cost of OMBR-RO-UV/H_2O_2 (USD 1.26 per m³) is already feasible for the reality of the USA. In the case of Brazil, it is feasible whenever water consumption per capita is above 21m³ per month, because then the water cost currently practiced jumps from USD 0.80 to 2.00 per m³ produced. However, since the cost of OMBR-RO-UV/H_2O_2 is still 73% more expensive than its MBR-RO-UV/H_2O_2 counterpart, there is space for cost reduction, as discussed in the following item.

Sensitivity analysis

In order to determine the importance of the FO membrane permeability, FO membrane cost and DS osmotic pressure in relation to costs and thus minimum cost of water production, a sensivity analysis was made. This analysis is important because, by identifying the most important factors, it indicates which ones should be prioritized when taking actions to reduce costs.

Different values for each of these factors were considered, and the resulting minimum water cost for each value was calculated whilst maintaining all other parametres constant (same to those informed in item 2.3 of this section)

FO membrane permeability

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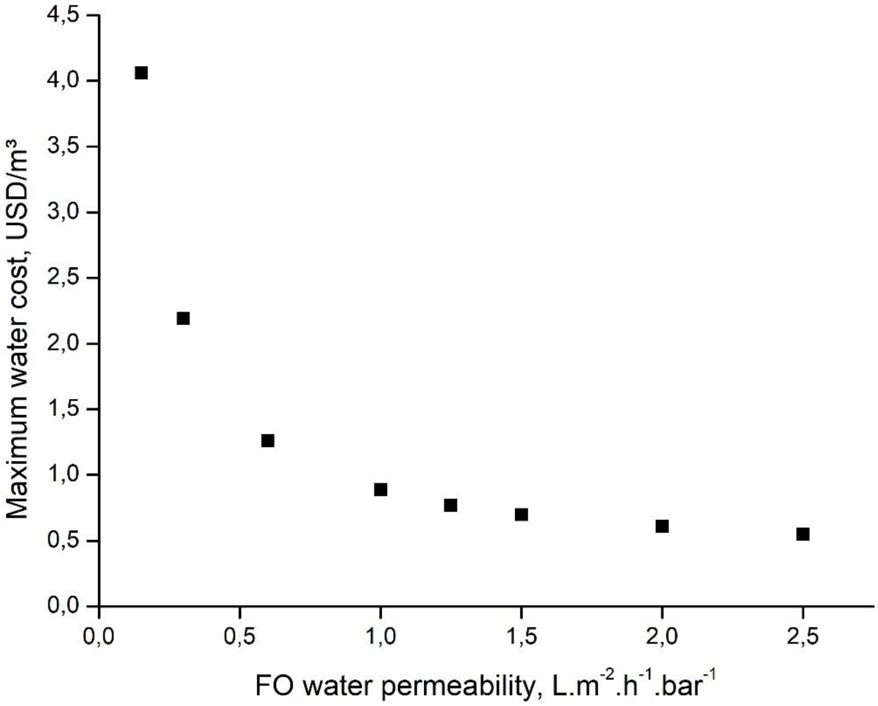
[13] Source: https://www.circleofblue.org/waterpricing/, accessed November 16th, 2020.

[14] Source: Basic Sanitation Company of the State of São Paulo (SABESP), considering an exchange rate of 1USD = 5.3 R$.

Figure 27 shows the results considering a permeability range from 0.15 to 2.5 L.m^{-1}.h^{-1}.bar^{-1}.

Figure 27: Sensitivity analysis for FO membrane permeability.

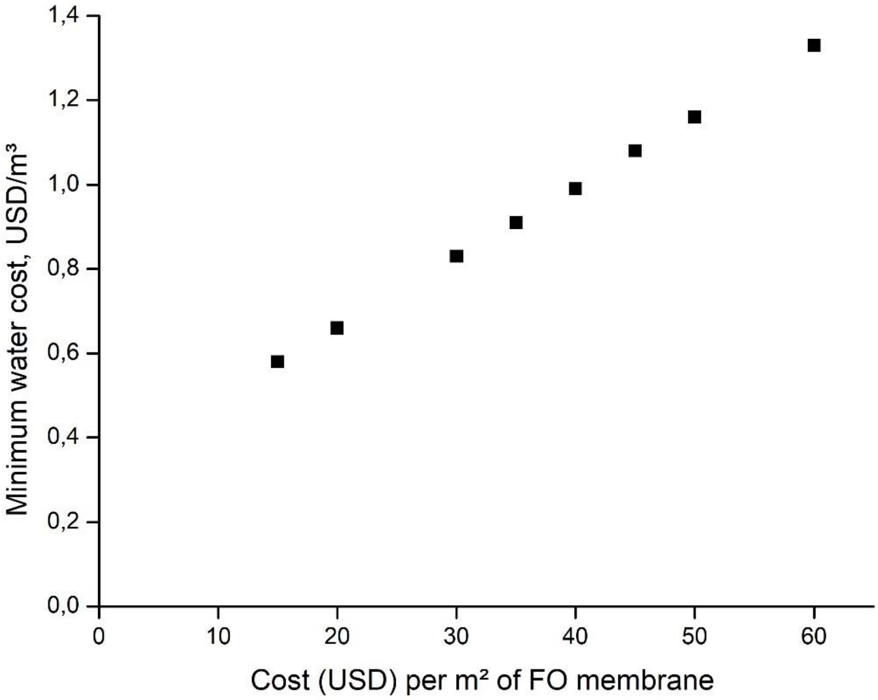


It is observed that water permeability greatly influences the minimum cost of water produced only up to 1 L.m^{-1}.h^{-1}.bar^{-1}. Therefore, the goal in OMBR research when aiming membrane synthesis is to guarantee a water permeability of 1 m^{-1}.h^{-1}.bar^{-} in the operating conditions of the bioreactor, for example, by reducing the concentration of internal polarization of membranes by minimizing the S of the porous support layer (as discussed in section Chapter 3, section "Factor affecting mass transport").

FO membrane cost

Figure 28 shows the results considering a cost range of USD 15-60 per m² of FO membrane.

Figure 28: Sensitivity analysis for FO membrane cost.

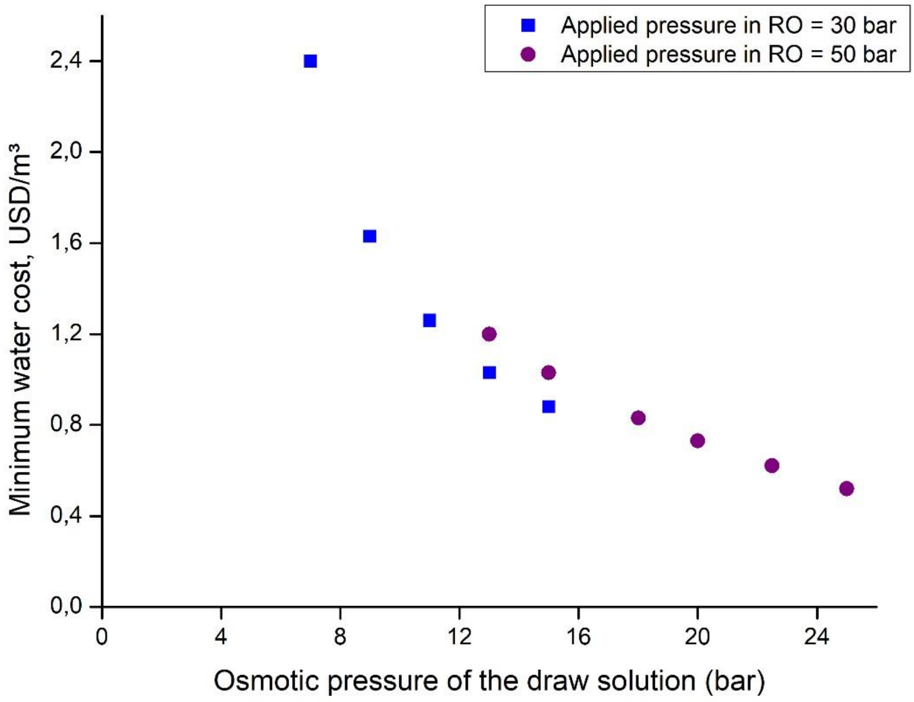


Processes involving FO membranes are not yet fully commercial and, therefore, the production of membranes and modules can be considered more expensive at the moment than RO membranes, which have been on the market for years. If, with the advancement of FO processes, they become more widely commercialized, one can expect that the price per m^2 would decrease. If it decreases to USD 40 per m^2, minimum cost of water produced would decrease to USD 0.99 per m^3 treated without any other improvements in the process, as shown in Figure 28.

DS osmotic pressure

Figure 29 shows the results considering different osmotic pressure in the DS whilst keeping osmotic pressure of mixed liquor set at 3.50 bar.

Figure 29: Sensitivity analysis for different osmotic pressures in the draw solution and different applied pressures in reverse osmosis.



Osmotic pressures in the DS from 7 to 15 bar were tested for an applied pressure in RO of 30 bar, showing a decrease in the minimum cost of water as the osmotic pressure increases. This was attributed to the lower cost with OMBR due to the higher water flux obtained for the permeability of 0.6 LMH.bar^{-1}, leading to a reduction not only in the CAPEX of OMBR but also in the OPEX costs related to depreciation and membrane replacement. This reduction offset the higher cost of RO due to the higher osmotic pressure to be overcome for permeate production (according to Equation 26).

Considering this result, another scenario was also evaluated by increasing the RO applied pressure to 50 bar and evaluating osmotic pressures in the DS from 13 to 25 bar. The result shows that the cost of the minimum m³ was highter than in the previous scenario when the osmotic pressure was 13-15 bar, however, it further decreased substantially as the osmotic pressure was increased, eventually becoming cheaper than the minimum cost obtained by MBR-RO when the osmotic pressure was 22.5 bar. These result are attributed to the same reasoning described above. However, it is noted that as the osmotic pressure increases, the driving force for the reverse salt flux also increases, according to Equation 23, leading to increase in salinity build-up in the bioreactor. Thus, the assumption that the osmotic pressure of the mixed liquor is stable around 3.50 bar becomes increasingly unlikely. For this reason, the operation should prioritize lower osmotic pressures but which still obtains substantial gains in the minimum cost of m³ in relation to the base scenario, for example, operating with DS osmotic pressure around 18 bar with RO applied pressure at 50 bar. In this scenario, the minimum cost falls from USD 1.26 to USD 0.83 per treated m³, and when carried out in conjunction with the other changes discussed in the previous items, this cost may be further reduced.

4.4 Conclusions

It was proven that UV/H_2O_2 can be used successfully for the purpose of controlling PhACs accumulation in DS, proving the hypothesis of the Thesis, since UV dose of 816 mJ.cm^{-2} with H_2O_2 dose of 30 mg.L^{-1} was sufficient to remove >91% of all PhACs present in the DS. These results were achieved even with high concentrations of $K_4P_2O_7$ in the solution, although this salt reduces the degradation of PhACs due to an apparent scavenger power of the pyrophosphate anion. Moreover, treating the DS with UV/H_2O_2 is more economically advantageous than periodically changing the DS current.

CAPEX and OPEX results showed that, in the current stage of OMBR-RO with UV/H_2O_2 technology, the minimum cost of reuse water can be USD 1.26 per m³ treated. This cost is 73% higher than the cost obtained in the scenario with MBR-RO, but feasible considering the water prices currently practiced for residential water in both the USA and Brazil. A sensitivity analysis showed the importance of some parameters, that can have great variability, on the final cost of reuse water. Based on these results, for a cost reduction of OMBR-RO with UV/H_2O_2, the following actions can be done: i) focus research on the synthesis of FO membranes with water permeability of 1 L.m^{-1}.h^{-1}.bar^{-1}; ii) focus research to lower the cost of the FO membrane to at least USD 40 per m² of membranes; iii) operate OMBR with inlet osmotic pressure of DS of 18 bar and applied pressure in the subsequent RO at 50 bar.

Individually, each of these actions can bring the minimum cost of water to values between USD 0.83 to 0.99 per treated m³. However, if all these actions are taken combined, the final cost would be USD 0.56 per m³ treated, that is, cheaper than the minimum cost achieved necessary for MBR-RO-UV/H_2O_2, which is USD 0.73 per m³ treated, guaranteeing not only the feasibility but even attractiveness of this process from an economic perspective compared to MBR-RO-UV/H_2O_2, which confirms the hypothesis of the Thesis.

Chapter 5 - Final Considerations

The main objective of the Thesis was to present a comprehensive evaluation of the innovative process OMBR-RO-UV/H_2O_2 to treat synthetic wastewater, remove PhACS and produce high quality water for reuse. This comprehensive analysis was done from a technical perspective, including assessment of the quality of reuse water and operational considerations of OMBR-RO-UV/H_2O_2, as well as from an economical perspective. Therefore, the conclusions of the Thesis are:

- Regarding water quality, results from this Thesis show that some moderately biodegradable PhACs such as SMX and EE2 are removed with high efficiency (> 90%) by the conventional biological processes of activated sludge when optimum operating conditions are adopted to maximize removal, such as high hydraulic and solids retention time, high concentration of dissolved oxygen and biomass acclimation to the PhACs. However, removal of recalcitrants PhACs, like CBZ and DIF, is still low even with these conditions. Therefore, the subsequent treatment of UV/H_2O_2 as well as the combination of the biological process with forward osmosis membrane (OMBR), followed by RO, were evaluated to maximize the removal of PhACs. Both were able to obtain removals above 98% for all PhACs. However, when the membranes are used, there is also the advantage of effluent mineralization and high nitrite, nitrate and orthophosphate removal, whereas in UV/H_2O_2 there is no nutrient removal, and mineralization occurs only with great consumption of electricity and H_2O_2. Therefore, for scenarios where high removal of PhACs and also of organic matter and nutrients are required, as in applications of high quality reuse, membrane-based processes are preferred.

- Regarding water quality obtained by membrane-based processes, results show the OMBR-RO process reached higher removals of nitrite, nitrate, SMX, CBZ and DIF than those achieved by MBR-RO. In quantitative terms, the concentration of these compounds in the RO permeate after OMBR was 4, 10, 74, 6 and 4 times lower, respectively, than in the RO permeate after MBR. These results indicate an advantage of replacing an MBR with an OMBR when very high removal of PhACs, nitrite and nitrate is important for the reuse option, for example, for potable applications. Although the concentrations of nitrite and nitrate achieved by the MBR-RO process are already sufficient to meet potable water (drinking water) requirements, the introduction of OMBR removes even more of these undesirable compounds. PhACs are not yet regulated in potable water, but the higher removal achieved by OMBR-RO for these compounds will be advantageous when regulations are created. OMBR also introduces another restrictive membrane barrier in the processs, that can act as a safeguard in case of operating problems that temporarily decrease the removal of unwanted compounds, which does not happen in a conventional MBR-RO. Thus, OMBR-RO can be seen as a more resilient process, which is another advantage of this process. It is noted, however, that the water quality improvement in reuse water was not observed for all compounds: for EE2, the removal achieved by OMBR-RO was lower. Moreover, despite being a promising technology, OMBR-RO cannot be seen as a technology for complete removal (i.e. below method quantification limit) of PhACs and nutrients from wastewater, even with a double membrane layer of membranes (FO and RO).

- Operation of OMBR using potassium pyrophoshate solution as draw solution had operational advantage in terms of low salt permeability towards the bioreactor (0.05 LMH), even when using an FO membrane with less retention of salts than those frequently used for FO applications. Such result is promising, as it opens the possibility of using FO membranes with lower salt retention than those currently used, thus being able to increase the water permeability of the membranes but without creating excessive increase of the salinity build-up in the reactor. Alternatively, FO membranes more restricted to the passage of salt can be employed, and by using potassium pyrophosphate a very low reverse salt flux would be obtained.

- It was experimentally proven, for the first time, that there was an accumulation of PhACs in the DS during continuous operation, due to the permeation of these solutes from the mixed liquor through the FO membrane. The economic analysis showed that the treatment of this current rather than its continous replacement is the best option, and experiments proved that UV/H_2O_2 can be used successfully to reduce the concentrations of PhACs in the DS. UV dose of 816 mJ.cm^{-2} with H_2O_2 dose of 30 mg.L^{-1} was sufficient to achieve removals above 91% for all PhACS, despite pyrophosphate acting as a scavenger of hydroxyl radicals. Therefore, the UV/H_2O_2 stage was included in the cost estimates for a large-scale process that is continuously operated.

- The minimum cost of water per treated m³ produced by the OMBR-RO-UV/H_2O_2 was calculated considering CAPEX and OPEX costs, based on a plant capacity of 24,000 m³.day^{-1}, 20-year lifetime of the project, interest rate of 5.68% per year and operational assumptions regarding membrane permeability, cost of FO membrane and DS osmotic pressure. In this scenario, the minimum cost of reuse water is USD 1.26 per m³ treated, which is in the range of prices currently practiced for residential water in Brazil and the USA, however remains 73% more expensive than the minimum cost of water produced by MBR-RO-UV/H_2O_2. To reduce CAPEX and OPEX costs, the simultaneous adoption of three conditions will be necessary: FO membranes must have a permeability of 1 L.m^{-1}.h^{-1}.bar^{-1} , cost of USD 40 per m² of FO membrane and inlet osmotic pressure of DS in OMBR must be 18 bar with applied pressure in subsequent RO set at 50 bar. Once these conditions are met, minimum cost of reuse water becomes USD 0.56 per treated m³, cheaper than the minimum cost of MBR-RO- UV/H_2O_2, which is USD 0.73 per m³ treated, guaranteeing the feasibility of the project from an economic perspective.

These conclusions indicate that there is sufficient reasoning to support the continuity of research and development of OMBR, aiming to expand it beyond the bench scale. When very high removals of PhACs, nitrite and nitrate are important for the reuse option that is being considered, OMBR-RO becomes particularly advantageous due to the superior removals of these compounds achieved by the process. However, the following caveats should be made: i) it is of paramount importance for technical feasibility of this process the development of FO membranes that meet the permeability criteria (1 L.m^{-2}.h.$^{-1}$.bar^{-1}) while maintaining a low internal polarization concentration and cost around USD 40 per m² of membrane; ii) the results showed that the improvement in reuse water quality is not for all PhACs; and iii) despite its promising potential to alleviate rveerse salt flux, demonstrated in this Thesis, the effects of the use of potassium pyrophosphate as DS need to be further explored, especially in regards to the biological activity of biomass. Thus, the following suggestions for future work can be made:

- Development of FO membranes with water permeability of at least 1 L L.m^{-1}.h^{-1}.bar^{-1} and low propensity to internal polarization concentration, in compact modules whose final production cost may be close to USD 40 per m² of membrane. Larger water permeabilities are desirable to maintain a high FO permeate flux thus reducing CAPEX and OPEX costs. The minimization of the internal polarization concentration is essential for full-scale operation to be technically feasible, and can be achieved by modifying the porous support layer of the membrane. Preference should be given to the development of hollow fiber membranes, as hollow-fiber modules are more compact than plate-and-frame modules. The cost per m² at FO is important to improve the economic feasibility of the process.

- To further investigate quality of reuse water obtained by OMBR-RO and compare it to reuse water obtained by MBR-RO, while increasing the number of compounds under analysis, and considering other PhACs and other categories of emerging pollutants. Special attention should be given to estrogens estrone (E1), 17-β-estradiol (E2) and estriol (E3), since they have physical-chemical properties similar to those of estrogen EE2, and EE2 was the compound with the lowest removal in OMBR-RO. It is noted that the improvement in water quality can strongly impact process acceptance by key stakeholders, since it adds a new factor to be considered i.e. technical improvement in the process, not just potential economics savings. Therefore, there is still a lot of space for experimental investigations to demonstrate more definitively the extent of the benefits of employing OMBR-RO in terms of water quality. Questions that can be explored include which micropollutants have the best removal on OMBR-RO and which have the best removal on MBR-RO and what is the influence of different types of FO membrane on these removals.

- After developing a more suitable FO membrane, a new assessment of potassium pyrophosphate as DS can be made, particularly with regards to effects on biomass growth. Questions that can be explored include what is the salinity builudp obtained when using membranes developed specifically for FO, whether there is still effects on biomass growth under these conditions and, if so, whether this is due to the lack of acclimatization of the biomass to salinity or due to change in microorganisms metabolism due to osmotic stress, which may favor catabolism (substrate utilization) over anabolism (growth related biosynthesis).

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