REPUBLIC OF TURKEY

YILDIZ TECHNICAL UNIVERSITY

GRADUATE SCHOOL OF SCIENCES AND ENGINEERING

INTEGRATION OF A MEMBRANE BIOREACTOR TO NANOFILTRATION/REVERSE OSMOSIS FOR TREATMENT OF EMERGING PHARMACEUTICALS IN DOMESTIC WASTEWATER

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Raghad Asad ALOBAIDI

Signature

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Dedicated to my Parents

Brothers and Sisters

and my Family

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Firstly Praise be to ALLAH almighty who bestowed me with courage, strength, and blessings all the route until finalizing this work. This thesis presents a step-by-step approach to explore MBR techniques. Systematically focusing on some hazardous concentrations of pharmaceuticals with substantive processes to reduce the effect of the latter on the environment.

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LIST OF SYMBOLS

A	Area
atm	Atmosphere
Cm	Centimeter
C	Concentration
Xss	Concentration of Suspended Solids
Ssoluble	Concentration of the Soluble Part of the Micropollutants
m3	Cubic Meter
Da	Dalton
C^o	Degree Centigrade
J=LMH	Flux
g	Gram
H	Hour
Kpa	Kilopascal
l	Liter
m	Meter
μg	Microgram
μm	Micrometer
mg	Miligram
ml	Mililiter
min	Minute
nm	Nanommeter
Kbiol	Pseudo First Order Reaction Rate Constant
t	Time
V	Volume
w/v	Weight Over Volume

LIST OF ABBREVIATIONS

ATN	Atenolol
BAPs	Biomass Associated Products
BOD	Biochemical Oxygen Demand
BZF	Bezafibrate
C	Carbon
CAPEX	Capital Expenditure
CAS	Conventional Activated Sludge system
CASPs	Conventional Activated Sludge Plants
CBZ	Carbamazepine
COD	Chemical oxygen Demand
CTP	Conventional Treatment Plants
DCF	Diclofenac
DNA	Deoxyribonucleic Acid
EDCs	Endocrine Disrupting Compounds
EDGs	Electron Donatings
eff	Effluent
EMPs	Emerging Micropollutants
EPS	Extracellular Polymeric Substance
EWGs	Electron Withdrawings
F/M	Feed to Microorganisms
H	Henry's Constant
HRT	Hyraulic Retention Time
iMBR	Immersed Membrane Bioreactor

inf	Influent
kd	Solid Water Distribution Coefficient
Kow	Octanol Water Partitioning Coefficient
LCMS	Liquid Chromatography Mass Spectrometry
LOD	Limit of Detection
LOQ	Limit of Quantification
MBRs	Membrane Bioreators
MeOH	Methanol
MF	Microfiltration
MLSS	Mixed Liquor Suspended Solids
MLVSS	Mixed Liquor Volatile Suspended Solids
MPs	Micropollutants
Mw	Molecular Weight
MWCO	Molecular weight cutoff
N	Nitrogen
NF	Nanofilteration
NGS	Next Generation Sequence
OPEX	Operating Expenditure
OTU	Operational Taxonomic Unit
PCR	Polymerase Chain Reaction
PCT	Paracetamol
PES	Polyethersulfon
Pka	Acid Dissociation Value
PPCPs	Personal Products Care & Pharmaceuticals
R.E.	Removal Efficiency

R_C	Cake Resistance
R_M	Membrane Resistance
RNA	Ribonucleic Acid
RND	Ranitidine
RO	Reverse Osmosis
R_P	Pore Blocking Resistance
RSD	Relative Standard Deviation
R_T	Total resistance
sMBR	Submerged Membrane Bioreactor
SMP	Soluble Microbial Products
SPE	Solid Phase Extraction
ss	Suspended Solids
TKN	Total Kjeldahl Nitrogen
TMP	Transmembrane Pressure
TSS	Total Suspended Solids
UF	Ultrafiltration
VAPs	Utilization Associated Products
WWTP	Wastewater treatment Plant

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ABSTRACT

INTEGRATION OF A MEMBRANE BIOREACTOR TO NANOFILTRATION/REVERSE OSMOSIS FOR TREATMENT OF EMERGING PHARMACEUTICALS IN DOMESTIC WASTEWATER

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Department of Environmental Engineering

Doctor of Philosophy Thesis

Supervisor: Prof. Dr. Özer ÇİNAR

Though conventional biological treatment plants can remove the basic pollutants, they are found to be ineffective in removing recalcitrant pollutants. Membrane bioreactors are considered a promising technology by having advantages such as higher effluent quality and producing low sludge in comparison to conventional biological treatment processes. In this study, the elimination of pharmaceutical compounds was investigated by membrane bioreactors under different solid retention time (SRT). The effect of SRT on the elimination of emerging pharmaceuticals was observed for 20, 30, and 40-day SRT and monitored for 96 days for each and, it was found that the 40-day SRT had the optimum performance in terms of the pharmaceuticals' elimination. Chemical oxygen demand (COD) removal efficiencies for each selected SRT were higher than 96% at steady-state conditions. The highest degradation efficiencies were observed for paracetamol, and when it is sorted from the most removed compound towards the lowest, it can be listed as Paracetamol, Ranitidine, Atenolol, Bezafibrate, Diclofenac,

Carbamazepine. The microbial community at the phylum level was also analyzed to understand the biodegradability of pharmaceuticals. It was noticed that the proteobacteria phylum increased from 46.8% to 60.0% after 96 days after adding the pharmaceuticals. Actinobacteria class which can metabolize paracetamol, carbamazepine, and atenolol was also increased from 9.1% to 17.9% after adding pharmaceuticals. The by-products of diclofenac, bezafibrate, and carbamazepine were observed in the effluent samples. The transmembrane pressure TMP was monitored during the whole work period and it was observed that during the 20 day SRT phase, the fouling occurred much more often and faster for both 0.2 μm and 0.45 μm membranes than the fouling occurred during the 30 and 40 day SRT phases. This might be due to the increase in the values of SMP and EPS when decreasing the SRT. The combination of MBR treatment to the NF270, NF90 and RO membranes resulted in the removal of four pharmaceuticals (paracetamol, ranitidine, atenolol, and bezafibrate) to below detection limits. In addition, it's worth noting that when the BW30 was used in conjunction with the MBR treatment, the removal efficiency for diclofenac and carbamazepine was higher than other membrane combinations recording about 86% and 82% respectively.

Keywords: Membrane Bioreactor, Pharmaceuticals, By-products, Solid Retention Time, Solid Phase Extraction.

ÖZET

Mikrokirletici İçeren Evsel Nitelikli Atıksuların Membran Biyoreaktöre Nanofiltrasyon/Ters Ozmos Entegre Edilmesi ile Arıtılması

Raghad ALOBAIDI

Çevre Mühendisliği Bölümü

Doktora Tezi

Danışman: Prof. Dr. Özer ÇİNAR

Konvansiyonel biyolojik arıtma tesisleri, temel kirleticileri giderebilse de, inatçı kirleticilerin giderilmesinde etkisiz oldukları tespit edilmiştir. Membran biyoreaktörler, geleneksel biyolojik arıtma proseslerine kıyasla daha iyi atık su kalitesi ve düşük çamur üretimi gibi avantajlara sahip olması sebebiyle gelecek vaat eden bir teknoloji olarak kabul edilmektedir. Bu çalışmada, farklı solid retention time (SRT – Katı bekletme süresi) altında membran biyoreaktörler ile farmasötik bileşiklerin giderimi araştırılmıştır. SRT'nin farmasötiklerin bozundurulması üzerindeki etkisi 20, 30 ve 40 günlük SRT kullanılarak her biri için 96 gün boyunca izlenmiştir. SRT'nin 40 gün olduğu çalışmanın, farmasötiklerin bozundurulması açısından optimum performansa sahip olduğu bulunmuştur. Seçilen her bir SRT için gözlemlenen kimyasal oksijen ihtiyacı (KOİ) giderim verimleri, kararlı durum koşullarında %96'dan daha yüksekti. En yüksek bozundurma verimi parasetamol için gözlendi ve en yüksek bozundurma veriminden en düşüğe doğru Parasetamol, Ranitidin, Atenolol, Bezafibrat,

Diklofenak, Karbamazepin olarak sıralanabilir. Farmasötiklerin biyolojik olarak parçalanabilirliğini anlamak için phylum düzeyindeki mikrobiyal topluluk da analiz edildi. Farmasötiklerle 96 gün sonra proteobakteri phylumun %46.8'den %60.0'a yükseldiği fark edildi. Parasetamol, karbamazepin ve atenolol'ü metabolize edebilen Actinobacteria sınıfı da ilaç eklendikten sonra %9.1'den %17.9'a yükseldiği gözlenmiştir. Atık su numunelerinde diklofenak, bezafibrat ve karbamazepine ait yan ürünler tespit edilmiştir. Transmembran basıncı TMP, tüm çalışma periyodu boyunca izlendi ve 20 günlük SRT fazı boyunca, hem 0.2 μm hem de 0.45 μm membranlar için kirlenmenin, 30 ve 40 günlük SRT fazlarında meydana gelen kirlenmeden çok daha sık ve daha hızlı meydana geldiği gözlemlendi. Bunun nedeni, SRT düşürülürken SMP ve EPS değerlerinin artması olabilir. NF270, NF90 ve RO membranlarına MBR tedavisinin kombinasyonu, dört farmasötik maddenin (parasetamol, ranitidin, atenolol ve bezafibrat) tespit sınırlarının altına düşmesiyle sonuçlandı. Ek olarak, BW30 RO membranı MBR prosesi ile birleştiğinde, diklofenak ve karbamazepin için bozundurma veriminin, sırasıyla yaklaşık %86 ve %82 olduğu ve, diğer membran kombinasyonlarından daha yüksek olduğunu belirtmekte fayda vardır.

Anahtar Kelimeleri: Membran Biyoreaktör, Ilaçlar, yan ürünler, Katı Tutma Süresi, Katı Faz Ekstraksiyonu

1
INTRODUCTION

1.1 Literature Review

It is well understood that many areas in the world have insufficient water supplies. For this reason, in certain areas, wastewater reuse is a normal application and the authorized agencies follow several protocols of intervention to facilitate its reuse. Regulations enforcing the reuse of recycled wastewater are as well very challenging in terms of removal efficiency and quality and health, this has led to new water treatment and purification systems being implemented. The use of ultrafiltration and microfiltration membranes, which are commercially feasible for high-quality purified water, is one of the latest new developments. The membrane bioreactors (MBRs) technology has achieved a significant level of wastewater treatment in the last two decades and is likely to expand. MBRs are rather compact and effective systems for separating suspended and colloidal matter and are a significant technological choice for wastewater reuse. This system should follow the highest quality requirements for clarification and disinfection of effluent. The benefits of this mechanism are well recognized in comparison to the conventional activated sludge process [1]. One of the most mentioned is the decrease in sludge generation due to high solid retention time (SRT) applying. Organic micropollutants causing environmental contamination are a serious issue now, particularly where it will be affecting the water bodies. The emphasis on micropollutants in the context of comprehensive agricultural and industrial projects is extended to micropollutants from different chemical groups, such as pesticides, personal care products, pharmaceuticals, industrial chemicals identified in trace concentrations. At the same time, the importance of micropollutant detection was highlighted by the establishment of biotests which revealed that certain micro-pollutants had highly biological activity. Micropollutants are found in river

water worldwide and wastewater is described as a significant discharge route. Likewise, additional pollution is caused by leaching from sites of solid waste, air deposition, and so on. While the presence of pharmaceutical compounds is so limited in the environment, knowledge of the long-term threats to aquatic species and human health even at low levels of drugs remains lacking. The increasing concentration and effect of micropollutants on the environment and, perhaps, human beings have increased over the past few decades or so. Many micropollutants are persistent, are only partially removed during treatment, and thus, when disposed of in the environment over a long period, have substantial pollution. By coming into force to establish a global framework, the European directive, Water Framework Directive 2000/60/EC underlines the importance of micropollutants in superficial water (rivers and lakes), transitional water (estuaries), coastal waters, and groundwater.

1.2 The Objective of the Thesis

As several studies have stated, the elimination of certain pharmaceuticals compounds during conventional wastewater treatment systems is very poor and as a consequence, they are present in surface, ground, and even drinking water ([10]; [11]; [12]). Therefore, there is an increasing need to improve effective methods of wastewater treatment, which allow efficient removal of emerging pollutants at trace levels. In wastewater treatment, the MBR system is more widely used nowadays because of its higher efficiency of effluent quality. The application of membrane bioreactor coupling to nanofiltration membrane or reverse osmosis (MBR–NF/RO) for water treatment is effectively implemented for the treatment of crude wastewater and secondary effluent to provide recycled water and also for the domestic wastewater treatment [13]; [14]. The latter studies illustrated that combining MBR and RO produced excellent effluent purity, with 99.99%, 99.72%, and 97.3% removal of (SS), turbidity, and (COD), respectively. It is thought that the application of (MBR–NF/RO) is excellent because of the simplicity of the installation and operation of the membranes and the advantages such as separation without phase change, the need

for little labor and also their modules design, maintenance are easy. In particular, (SMP) and (EPS), which were defined as two key issues influencing membrane fouling in aerobic MBR, should be investigated furthermore in the MBR system to better understand membrane fouling mechanisms. Given these thoughts, the purpose of this study is:

1- The development of a sensitive multicomponent solid phase extraction method to analyze by LC/MS-MS for the simultaneous analysis of 6 different therapeutic classified pharmaceuticals in synthetic domestic wastewater.
2- Evaluate the impacts of SRT on the Aerobic MBR treatment efficiency in terms of removing these pharmaceuticals from the synthetic domestic wastewater.
3- Evaluation of the contribution of NF/RO in the removal of these pharmaceuticals.
4- At different SRTs, the mechanism of membrane fouling is illustrated in terms of the influence of biomass concentration, SMP, and EPS.
5- Also, variation of microbial species due to micropollutants was detected in the study.

With the knowledge and experience gained at the end of the project, contribution and knowledge will be provided to the MBR systems to be established in the country in near future. In addition, a new approach will be given to the treatment of organic micropollutants and the improvement of filtration performance in wastewater. In addition, depending on the study results, the integrated MBR- NF/RO production will start in the country for wastewater reclamation and reuse. The work to be done in the field of NF/RO membranes will open the way for the establishment of these systems in Turkey in the future. Thus, membrane technologies in wastewater treatment will be included in alternatives. The conflict to be done will speed up the handling of issues such as the design and operation of MBR systems as well as minimizing the energy and labor issues.

By obtaining new approaches to the treatment of emerging micropollutants, the treatment of such wastewater will become easier and can be used easily even in small settlements. In this way, protection of water resources which is a national wealth will be provided.

1.3 Hypothesis

Although traditional water and wastewater treatment plants are successful in controlling pollutants such as organic substances and nutrients, they cannot manage to remove the micropollutants (MPs). These micropollutants are substances found in low concentrations (ng/L and μg/L) in water and wastewater and consist of metals, hydrocarbons, surfactants, hormones, and pharmaceutical products. According to many studies, conventional wastewater treatment systems are insufficient to degrade certain pharmaceutical compounds, as a result of which they can be found in surface and groundwater [15];[16];[17]. In particular, pharmaceutical compounds are biologically active compounds and affect microorganisms upon their discharge to the aquatic environment. They are recalcitrant compounds that take a long time to break down in nature, therefore, effective methods of wastewater treatment that allow efficient removal of emerging pollutants at trace levels are increasingly needed. In wastewater treatment, MBR (membrane bioreactor) systems are more commonly used recently because of their higher effluent quality performance. MBRs are effective in the treatment of many organic and inorganic pollutants, offering 3 main advantages, involving (i) enhanced adsorption capacities by the improving of biomass characteristics; (ii) improved higher sludge biodegradation through the microorganisms' retention, (iii) direct removal of several contaminants adsorbed on rejected particles through the membrane [18].The benefits of these processes are commonly recognized over the conventional activated sludge process[19]; the most cited one is the decrease of sludge production resulting from operation at high solid retention time (SRT). In general, hydrophobic and readily-biodegradable contaminants are very effectively eliminated by MBRs. However, hydrophilic

compounds, in particular biodegradation-resistant ones, may not be included [20]. The substantial difference in MBR removal efficiency for several pharmaceuticals, from near-complete removal (e.g. paracetamol and bezafibrate), to almost no removal, for some others (for example, carbamazepine and diclofenac) [21].

Bacterial degradation, and/or sorption are the main mechanisms to eliminate micropollutants from wastewater through treatment. They are stated to be the most dominant mechanisms. Even so, methods of micropollutant elimination do not obey a common guideline because their proportional contribution relies upon the micropollutant physicochemical properties, the wastewater sources, and specification, as well as the operating parameters of the wastewater treatment plant. An important issue is to consider why the performance of membrane bioreactors (MBR) relevant to the micropollutants removing like pharmaceuticals is influenced by the treatment conditions imposed in terms of the sludge retention time. Nevertheless, indeed one compound differs in removal rate and is associated with the physicochemical characteristics of xenobiotics

Various analytical determination methods of pharmaceutical compounds in wastewater are already available in the literature and have recorded specific pharmaceutical existence at ranges of ng/L to g/L [22]. Multi-residual analytical methodologies, including pharmaceutical products of the multi-class range, become however the tools required for providing reliable and broad knowledge on their presence and for monitoring their removal, partitioning, and final fate. When analyzing several different physicochemical compounds simultaneously, the high recovery rate for each compound may not be seen. Therefore, a common experimental condition must be determined. However, the creation of the multicomponent analysis method is rewarding due to the reduced number of analyses to be performed in routine analysis. The pre-concentration and isolation of the goal analytes can be performed by (SPE). The determination of the overall SPE method is important because most of these multicomponent analysis methods consist of two or

more different sorbent materials, solvents used for elution, and involve grouping target chemicals according to their physicochemical characteristics.

1.4 Membrane Bioreactor (MBR) Technology

MBR technology is considered to consist of conventional activated sludge treatment along with a filtration process by using a membrane of a pore size ranging from 10 nm to 0.4 microns (micro/ultrafiltration), which enables sludge separation. The membrane acts as a barrier, preventing all molecules, colloids, pathogens, and viruses from the treated water while disinfecting it completely. Besides that, it might apply over a wide sludge concentration (up to 12 g/l instead of the common 4 g/l in conventional systems), decreasing reactor size and sludge generation significantly. Typically, MBR is classified into two groups based on their setup; side stream membrane bioreactor and submerged membrane bioreactor (sMBR). The membrane module is placed outside of the bioreactor in the side stream membrane bioreactor, (Figure 1.1-b2). The membrane module in a submerged membrane bioreactor is immersed in the bioreactor, enabling the permeate to flow out when the sludge is retained (Figure1.1-b1). Aeration in the sMBR supplies oxygen, keeps the activated sludge in suspension, scours the membrane surface, and reduces fouling. The submerged configuration is the most commonly implemented in domestic wastewater treatment because of reduced operating expenditures [2].

1.5 Advantages and Challenges

For wastewater treatment and reuse, MBRs constitute a significant technological choice, as previously mentioned, as they are very compact and effective systems for separating suspended and colloidal particles and making better effluent quality, disinfected water to be accomplished. Full biomass retention in the aerobic reactor, which is separating (SRT) from (HRT), is a massive benefit of these MBR systems, High water quality in terms of COD, nitrogen, phosphorus, and ammonia, preservation of suspended solids and microorganisms, consistent biomass contents,

and effective treatment of variable wastewater are some of the other benefits of MBR. The system is also more compact to install than a conventional activated sludge system (CAS) since it eliminates three existing processes from the conventional design, and the input wastewater just requires to be screened prior to removing the coarse solids which might fracture the membrane. (Figure 1.1).

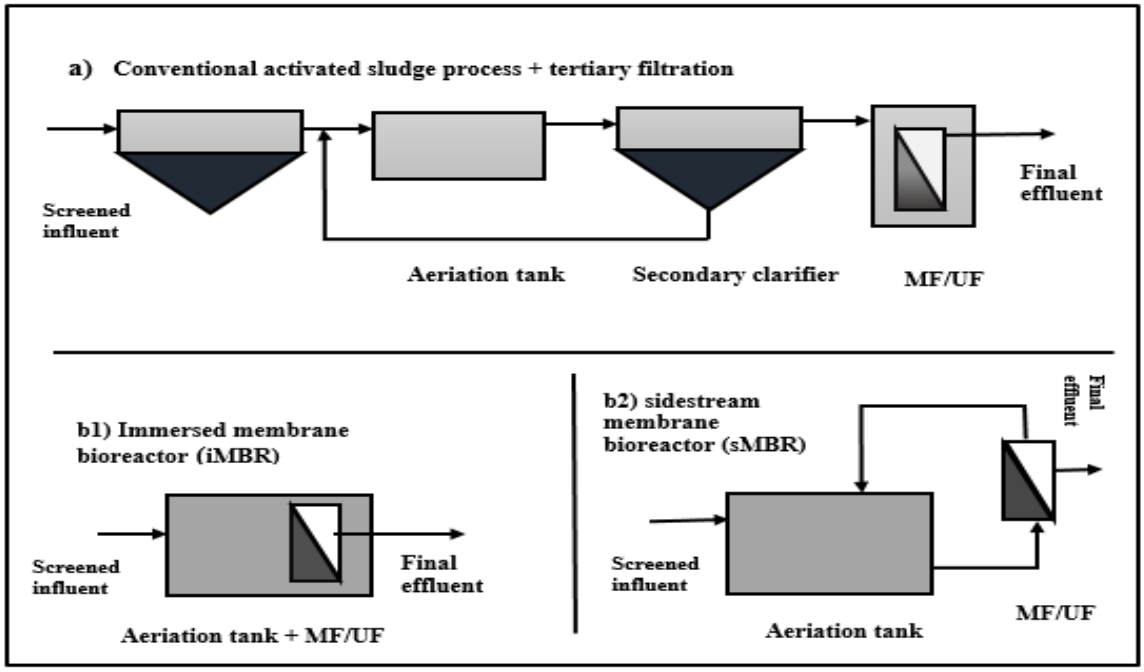


Figure 1.1 Conventional Activated Sludge System (a) and MBR in Both Configurations: Immersed (b1) and Sidestream (b2) [3]

Despite the obvious advantages of MBRs, their extensive use is restricted by their higher cost, both capital and operating expenditure (CAPEX and OPEX), which are primarily due to membrane installations and maintenance, as well as high power consumption. Fouling occurs when solids accumulating on the membrane surface during operation obstruct, occlude, or block membrane pores, causing permeability reduction of the membrane. The existence of particles and macromolecules of quite varying sizes, as well as the biological content of the microbial suspensions, contribute to the phenomenon's complexity, leading to a highly heterogeneous system. Besides that, the filtration process's complex behavior adds a specific complexity to the fouling mechanism. [4]. Moreover, permeability loss may result

from the accumulation of solid matters in the pores of membrane modules, which is called channel clogging as a result of local crossflow conditions breaking down. Other operational problems include the difficulty of membrane systems (involving particular cleaning protocols), the ability to create foam (due in part to excessive aeration), the lower sludge dewatering capability, and the highly sensitive to shock loads.

The following is the operating techniques for the submerged configuration to avoid membrane fouling (which has a direct or indirect effect on CAPEX and OPEX):

1. choosing a suitable permeate flux
2. scouring the surface of the membrane by aeration
3. implementing physical cleaning methods, including backflushing (while the effluent is applied to wash the membrane reversely) and relaxation (when no filtration occurs), in addition
4. implementing chemical cleanings procedures, of varying frequency and intensity (recovery cleaning and maintenance cleaning).

1.6 Design and Operation Consideration

As stated earlier, the sMBR seems to be the commonly used configuration for different purposes. Some design and operation concerns should be mentioned here such as:

1. Pretreatment
2. Flux design
3. Control of membrane fouling and cleaning
4. Solid retention time (SRT)
5. Membrane life

1.6.1 Pretreatment

Membranes are highly susceptible to harm from rough solids like leaves, plastics, and rags, as well as small particles such as hair in wastewater. A shortage of efficient pretreatment/screening was already established as a significant technological issue of MBR installation [5]. Fine screening is often necessary for such a purpose to protect the membranes.

1.6.2 Flux Design

Membrane permeate flux is a critical design and operating parameter with significant CAPEX and OPEX implications. The ideal operation flux values for different full-scale iMBRs often used in domestic wastewater treatment have already been reached. 19-20 l/h m^2 [1] with a maximum flux in the scope of 37-73 l/h m^2 [6].

If the mean pattern of the design peak net flux and operation averaged flux has marginally risen, consider the effect of this difference on CAPEX (i.e. more membrane surface demand) and OPEX (i.e. more membrane replacement expenditures).

1.6.3 Membrane Fouling Control and Cleaning

It is commonly believed that considering membrane fouling is essential for optimal MBR operation. Fouling reduction contributes to higher energy needs and has been the major contributor to OPEX. [7]. The complexity of this phenomenon has resulted in restrictive plant designs where the needed power is too difficult to be highly optimized. Most MBR implementations have introduced common fouling reduction procedures such as air sparging, physical cleaning protocols (i.e. backflushing and relaxation), and chemical cleaning as a basic operation strategy to reduce fouling.

1.6.4 Sludge Retention Time (SRT) and Biomass Concentration

SRT helps to improve performing efficiency and membrane filtration. Accurately, this parameter focuses on biomass concentration (MLSS), production of (SMP), and the performance of oxygen transport. Raising the SRT reduces the bioreactor volume needed by increasing the sludge solids concentration. As a result of the slow growth

rate of certain microorganisms (specifically nitrifying bacteria), a higher SRT results in higher performance efficiency and less sludge production. Furthermore, it has been indicated that increasing SRT values improve membrane permeability by lowering SMP generation. High solids concentrations, on the other hand, cause the microbial suspension to become more viscous, lowering air sparging ability and oxygen transport rate to the microorganisms, leading to greater power consumption besides increased membrane fouling and the chance of membrane blockage. For these causes, and for financial purposes, the majority of full-scale systems are constructed for MLSS of 8-12 g/l and SRT of 10-20 days. [8].

1.6.5 Membrane Life

Regarding that MBR is a rather new technology the information regarding its life expectancy is rather limited, however, some researchers estimate the life of membrane would extend to 10 years [9].

2
GENERAL INFORMATION

2.1 Wastewater Treatment by MBR

Membrane bioreactor technology has been in use for approximately 50 years, with Dorr Oliver commercializing the first sidestream MBR design in the late 1960s. [23]. Even so, it has only been in the last 30 years that there has been a substantial increase in its adoption and the resulting expansion of the municipal market, which happened to coincide with the development of the immersed configuration (iMBR) [1]. Legislation, which sets limits for, among other things, disposal water quality and freshwater extraction, is generally acknowledged as a major force for the development of municipal water and wastewater treatment systems. Legislation is influenced by a variety of socioeconomic and other conditions, including water shortages and public opinion, and has favored wastewater reuse for nonpotable purposes as a way of conserving freshwater resources. Reuse is especially popular in areas with aging or in many cases non-existent, infrastructure that allows for treatment by large, centralized facilities. Because of the previously mentioned reasons, the MBR sector is being propelled. MBRs have had the most success within areas of water recycling and implements requiring high quality effluent content. MBRs are bioreactors that combine conventional biotreatment with membrane filtration on the outside or inside of the reactor. The most frequently observed advantages of MBRs over CASPs are well-known, and the ones most frequently named are [1]:

- Product water of high treated, clarified, and mostly disinfected,
- Plant with a small footprint,
- Independence in terms of liquid and solids residence times,

- Desirable biological condition for biotreatment, especially for the removal of ammonia, and
- Waste sludge production is reduced.

Of these, the smallest environmental footprint and better treated water quality are normally the most realistic considerations. In a conventional sewage treatment plant, an MBR replaces three unit operations: primary sedimentation, secondary biological treatment, and tertiary filtration/disinfection. As a consequence, it is generally easier to control the biotreatment process. Despite the fact that the immersed configuration is now available, MBR technology is subjected to high capital and operational costs, and also the negative stigma related to relatively new technology. The lack of support from the government and limited allocation of capital in developing countries such as Asia and Latin America are limiting the penetration of the MBR sector, which is primarily supported by strategic partnerships and joint ventures [24]. In the case of wastewater treatment technologies in general, these are mostly common attributes including efficiency (in terms of product effluent quality), operational simplicity, and durability. Capital, and operation and maintenance expenditures, primarily related to energy demand and membrane replacement [1], [25]. In the case of MBRs, Membrane fouling is a critical process aspect common to all membrane technologies. The elimination of most organic substances (protein, carbohydrate, etc.) and nutrients is the aim of wastewater treatment. Sorption and biodegradation of organics, as well as absorption of inorganics by activated sludge, occur in conventional wastewater treatment processes (CTP) and MBR processes. Activated sludge is primarily made up of flocculating microorganisms suspended in aeration tanks in contact with wastewater. The efficiency of wastewater effluent is significantly influenced by the biomass separation technique [26]. CTPs usually operate at 1–5 g/l MLSS, while MBRs operate at much higher concentrations, ranging from 8 to 25 g/l or even higher [27]. Due to the membrane separation step, MBR technology provides treatment for sewage at high MLSS concentrations and is not

restricted by the secondary clarifier's sedimentation capacity. To keep a steady microorganisms' concentration in the tank, excess sludge must be removed from the system as biomass increases. SRT, which is regulated by removing excess sludge, is one of the most important parameters in activated sludge systems to control treatment performance. High SRTs are usually associated with good wastewater treatment efficiency in terms of COD elimination. In MBR, SRT of up to 25 or 80 days is commonly used, while CTP values usually range from 8 to 25 days. Because of the high SRT values and complete solids retention within the MBR, microorganism biodiversity is favored, and even free-living bacteria and slowly growing bacteria are maintained in the system [26]. During the treatment process, wastewater passes through a screen, where coarse constituents are removed prior the reactor is turned on. Because the mechanism was kept in aerobic condition, the influent was exposed to aeration from the bottom of the chamber. Aeration causes active sludge within the reactor, and the released oxygen gas produces a shear and prevents the membrane pores from plunging, a process known as fouling. However, the presence of mixed liquor within the reactor exposed a vacuum that allowed treated water to be discharged to the outside.

2.2 Membrane Fouling in MBRs

Membrane fouling occurs when the permeability of the membrane decreases during MBR activity. It also refers to the rise in transmembrane pressure (TMP) during MBR operation at constant flux. Membrane fouling was generated by biocake formation on the membrane surface as a result of fluid motion of activated sludge and microbial growth, as well as pore blockage caused by small particles, colloids, and solute adsorption [28], [29]. When MBRs are run at constant flux, three stages of fouling are typically proposed: conditioning fouling (step 1) caused by a partial block of pores, and solutes adsorption, steady fouling (step 2) caused by biofilm formation and more pore closure, and the TMP jump (step 3) caused by one or more of the following mechanisms or a combination of them: (i) due to a continuous blocking of

pores, local flux starts to exceed the critical value and particles begin to deposit at an ever increasing rate; (ii) coagulation occurs in the first layers at a critical pressure; (iii) percolating colloids inside the cake reduce the size of the cake voids until connections are lost [30].

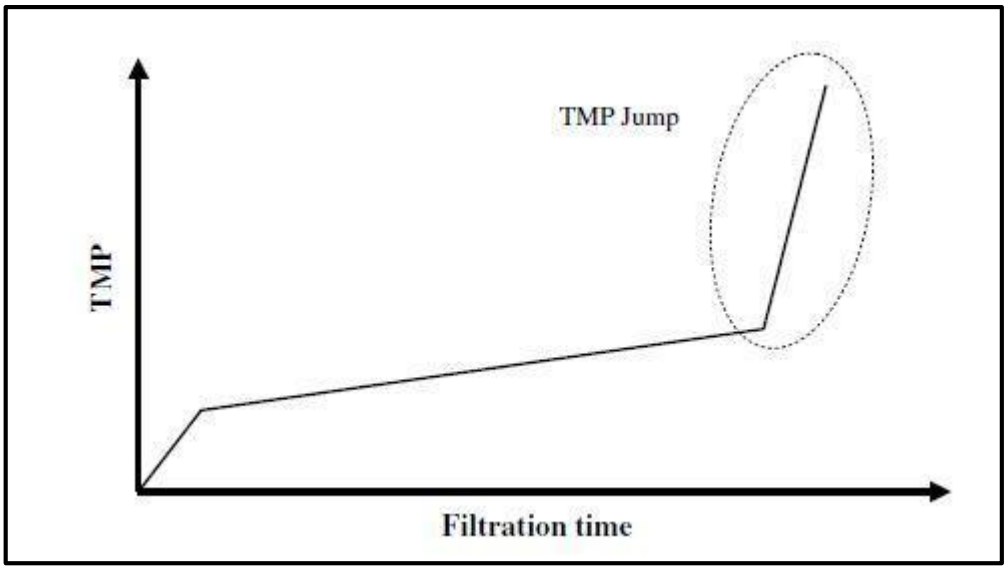


Figure 2.1 Schematic Illustration of the Long-term TMP Profile [31]

Many studies have found that the supernatant of activated sludge, which includes colloids and solutes, plays a bigger role in MBR membrane fouling than biological flocs. [32]. As a result, a lot of research has been done on fouling. Other more realistic aspects of MBR process operation, like clogging of membrane channels by massive solids. Chemically cleaning of the membrane has gotten a lot less coverage – most likely in opposition to the demands of practitioners. This is possible because academics have preferred to concentrate on preserving membrane permeability by potentially regulating foulant production rather than on process engineering. Membrane fouling, plugging, and cleaning are all aspects of membrane maintenance. Permeability is maintained mainly by membrane aeration.

Aeration is an essential factor for both the hydraulic and biological process components; it keeps solids suspended, supplies the biomass with oxygen, and shears the membrane surface. The two most important contributors to operational costs are membrane replacement and energy for aeration, which requiring between ten and fifty percent of total energy demand [25]. The effectiveness of aeration is determined by a variety of process design factors, including membrane module design, as well as the different types of aeration mode, and parameters of operation and maintenance. However, In terms of membrane module dimensions, there is a little range of commercial designs. Only stabilized circumstances are maintained in the field of operation to provide the unavoidable accumulating of foulants. With the aid of commonly used and well-known mechanisms that are based on previous research, filtration processes encapsulating:

- complete blocking
- standard blocking
- intermediate blocking
- cake filtration

The fouling mechanisms of complete blocking, standard blocking, intermediate blocking, and cake filtration are illustrated in Figure 2.2 According to the models described above, flux reduction is dependent on the proportion of particle size to pore size [33]. Standard blocking and cake filtration models appear to be the most relevant for predicting the primary flux reduction or protein filtration due to the colloidal particles filtration [34]. Filtration mechanisms have been subjected to scientifically justified information, and some have been chosen to be included within a framework of different important expected influences.

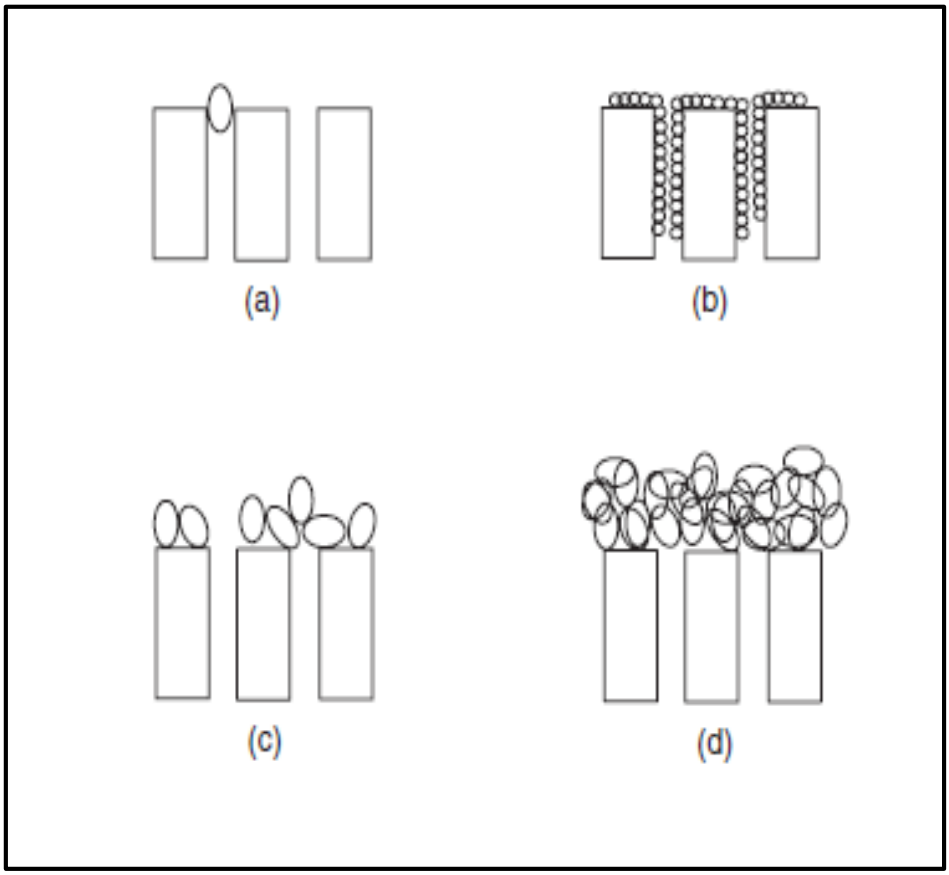


Figure 2.2 Complete Blocking (a), Standard Blocking (b), Intermediate Blocking (c) and Cake Filtration (d) [1]

Two distinct variations including TMP with constant flux phase and flux with constant pressure phase have to be monitored in the process application period to understand fouling in MBR systems. Many wastewater treatment plants, on the other hand, operate in a fixed flux phase, and fouling is detected later by monitoring the transmembrane pressure gradient over time. The first operational disturbance in MBR systems is a sluggish and partial increase in TMP, also known as the operation's early symptoms. Whether favorable cleaning methods were not used in the MBR process, a sudden rise in transmembrane pressure can be seen following the gradual increment in TMP.

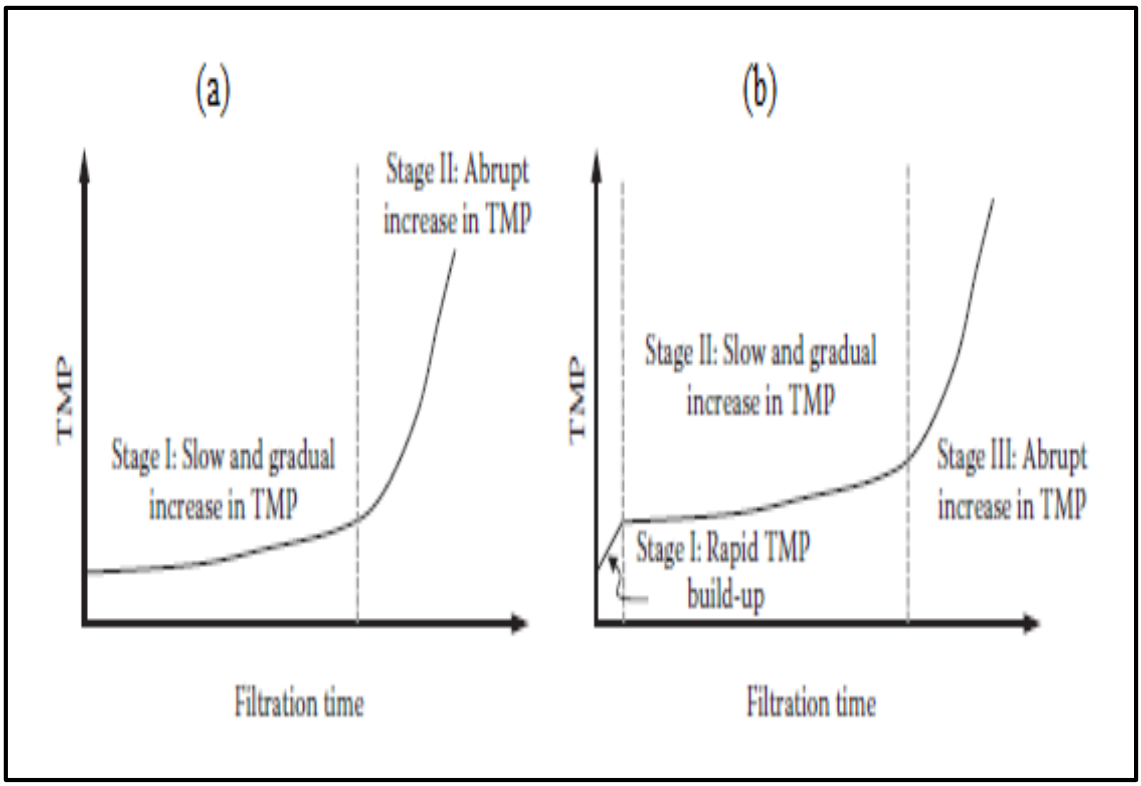


Figure 2.3 Sudden TPM Increase Contrived in MBR processes: (a) Two-phase of TMP Change and (b) Three-stage of TMP Change [35]

The two processes of incremental TMP increase and abrupt TMP change are illustrated in Figure 2.3 a. Two-phase TMP step-up is the term used to describe these forms of sudden changes. The time it takes to reach the broken point of a gradual line is influenced by the cleaning technique and how it is implemented. Cleaning methods that are more effective will expand the duration of abrupt change moment in TMP as well as the time of membrane utilization.

The abrupt changes are represented in three stages in Figure 2.3 b. TMP increasing is usually kept small and swift at the start of the MBR operation. The rapid plunging of the membrane and membrane pores by sludge molecules, concentration polarization, and membrane compaction at the mutational phases of the filtration process may cause the changes described above. The subsequent second stage increase sometimes obscures the first abrupt change in the TMP. As a result, a three-phased TMP change can be viewed as a two-staged TMP profile. The accumulation of

microbial flocs and particles on the membrane surface causes a sluggish and partial increase in TMP in the second phase of the TMP to acquire; in general, the initial stage of the plugging is the gradual cohesion of dispersive matters to the membrane surface and pores sides. Rapid TMP increment in the third step is associated with a reduction in porosity resulting from pressurization, which is happening on the cake layer during the process in combination with increased contents of EPSs built-in.

2.3 Fouling Rate

Fouling rate is a description that is applied for a definition of the fouling of the membrane. During the fouling process, four distinct phases can be established. These are the ones:

a. Plugging of the small pores

b. Covering of the internal sides of the larger pores

c. Thrusting of small particles and direct plunging of the larger pores

d. Cake layer formation

Since each fouling step is difficult to describe or quantify, verifying the overall fouling tendency is normally measured rather than defining each fouling step. The easiest way to get a sense of fouling tendency is to specify the fouling rate. The fouling rate is the simplest way to gain insights into the fouling tendency.

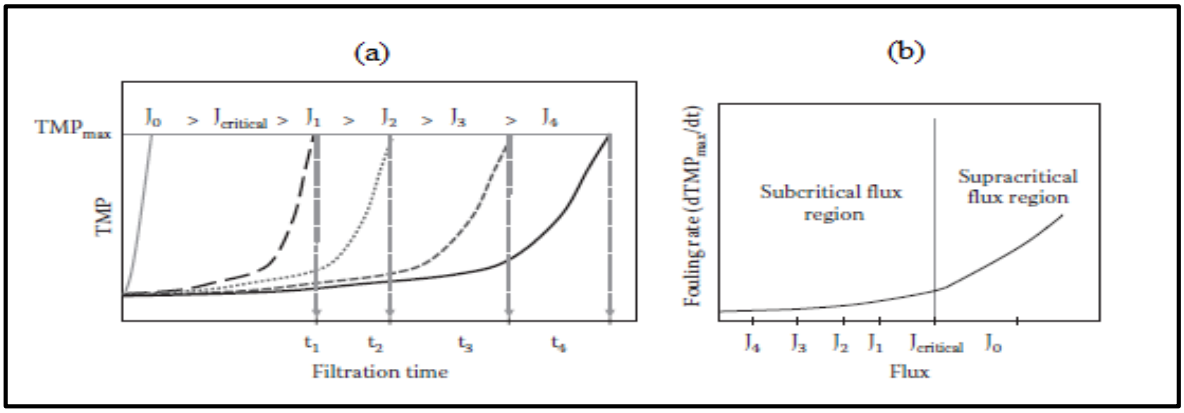


Figure 2.4 Typical TMP Increment Template (a) and Fouling Rate as a Function of Flux (b) [35]

The derivative form of the TMP increases by a substantial amount of time (dTMP/dt), as shown in Figure 2.4 a. The unit for the derivative pressure operation, on the other hand, should be kPa/h or psi/h. Instead of TMP, the capital letter 'R' could be used to describe the fouling propensity at a substantial time to make calculations for fouling resistance. The fouling rate unit, in this case, is m^{-1} h^{-1}. Additionally, the fouling rate is affected by the operation's flux rate, as illustrated in figure 2.4 b. When operational flux increases from J4 to J1, the fouling rate increases till it reaches Jcritical. The fouling rate increases abruptly outside the Jcritical zone, which is expressed as the supracritical flux region. Jcritical ranges in MBR plants for municipal wastewater processing are usually between 10 and 40 LMH, which distinguishes critical flux from sub and supracritical areas. The critical flux is varying depending on the types of influent used within the reactor.

2.4 Classification of Fouling

The fouling mechanism on membranes is hard to clearly comprehend and cannot be clarified by a single method. Studies have explored various types of ordinations of fouling in MBR processes. Fouling may be classified as mild, moderate, or extreme according to the classification measurements used and the application. The ordering of the membrane fouling in bioreactors is represented in figure 2.5. The most basic and easy way to classify fouling is to take account of flux reversibility just after an ordinary cleaning method. The fouling procedure is therefore divided into three types: reversible, irreversible, and irrecoverable. In the case of fouling problems, fouling may be classified in plugging, the generated cake layer, and internal pore plugging, depending on the second criterion.

The membrane plugging or block of membrane channels, however, is also not regarded as a membrane block, as it occurs externally on the surface of the membrane, by vehemently accumulating of the suspended solids within the mixed liquor. This decreases the membrane efficiency and leaves the membrane worse so

that the plugging is normal. The final criterion is the algorithm of the solid creation. This fouling

classification is made up because of the cake layer and the pore diameter reduction or the pore squeezing and the pore blocks. Although the membrane compaction is not classified as a mode of fouling, it decreases the membrane's filtration efficiency such as plugging.

2.5 Factors Affecting Membrane Fouling

Though it is very difficult to establish a specific order on membrane fouling in the bioreactor process, three factors significantly influence and drive the fouling as illustrated in Figure 2.6.

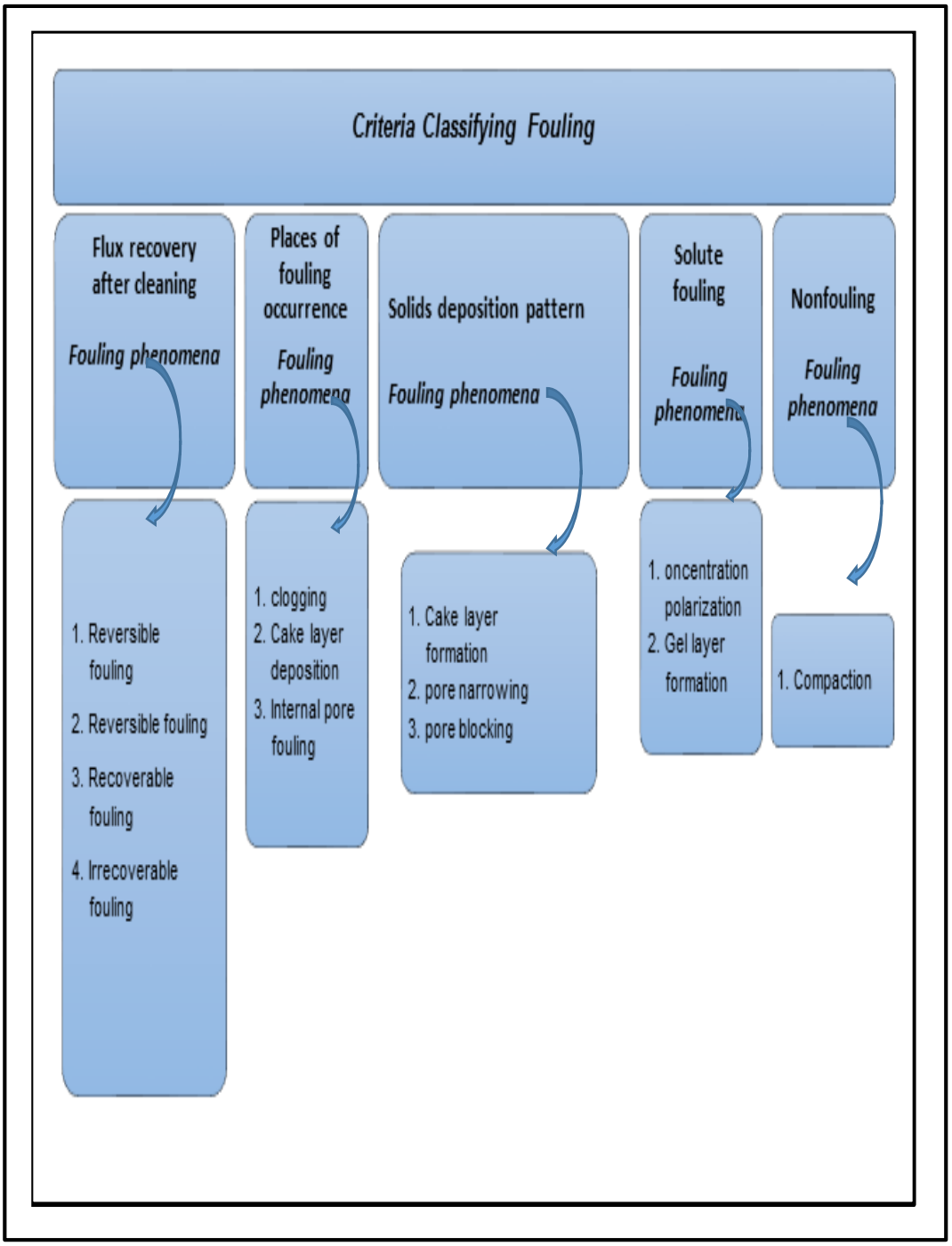


Figure 2.5 Classification of the Membrane Fouling in MBRs [35]

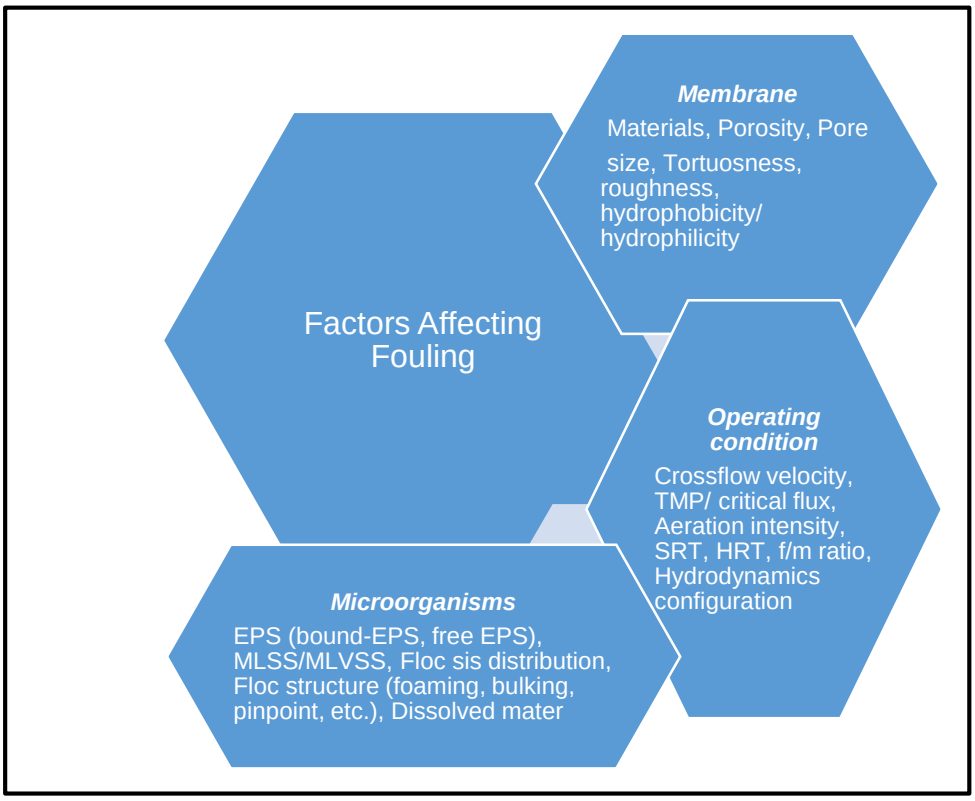


Figure 2.6 Factors Influencing the Membrane Fouling in Bioreactor Systems [35]

Individual fouling causes membrane fouling separately and/or reciprocally. They affect each other, as seen in the diagram. Important operating conditions like HRT and SRT, for example, have a direct influence on membrane fouling. They affect microbial properties instantaneously, such as EPS make-up or MLSS concentration, both of which are critical factors in causing membrane fouling.

2.6 SMP/EPS

Microbial organisms produce EPSs as a mucous-like constituent and well-known molecule because of their large size. They play an important role in floc formation and include a nonhomogeneous polymeric substance that encapsulates DNA and RNA in low amounts and polysaccharide, protein, lipid, and humic acid in massive amounts. Any of these substances have an important part in membrane clogging.

EPSs are rich substances with water that have a significant part in the effluent flow during the process. Through the infiltration process, the accumulating of SMP molecules causes an increase in TMP. The presence of proteins, polysaccharides, and other compounds increases the fouling rate as the production of SMP increases. Within the flocs, however, bound EPS molecules exist in a soluble state in an accumulated solution. Because of the foulant material's stopper operation, pores may become clogged, causing internal fouling problems in the instance of pore narrowing. When the membrane or support material is chosen correctly, this condition may be avoided. The cake formation over the membrane's surface is a product of dominant infiltration resistance. The process is based on bound EPS molecules, which closely maintain the internal structure of the cake layer and have an important part in permeate flow via the membrane surface. As a result, in MBR systems, bound EPSs are one of the most influential molecules.

2.7 MBR Technology and Micropollutants

The effectiveness of membrane bioreactors (MBRs) in terms of water quality is commonly controlled by the main, generally governed, elements of biochemical (and sometimes chemical) oxygen demand in water, ammonia, and suspended solids.

The amount of nutrients and the bacteriological composition can be controlled under some circumstances. MBRs are widely acknowledged as providing excellent water treatment. typically 4-6 times pathogenic bacteria removing, almost full removing of suspended solids and also decreasing ammonia or TKN to less than 1 mg l^{-1} [1]. Particles considerably smaller than the effective MW cut off of membrane, and non-biodegradable soluble substances, thus, pose a problem to the membrane permeate quality. Given that certain viruses are around the same size as a membrane pore size, so It's likely that MBR membranes won't reject them [36]. Both biotreatment and clarification processes are challenged by non-biodegradable soluble substances, as well as more recalcitrant micropollutant-bearing wastewaters. The process's ability to

remove such products is wholly reliant on (a) their tendency to sludge and (b) the membrane's selection. The MBR process's sensitivity, in combination with the higher biomass compositions at which they run and the separating of HRT and SRT, can be predicted to enable more biomass concentrations to adsorb soluble recalcitrant pollutants and retain them. The growth of a bacterial community at these long SRT periods is needed for biodegradation of these products, or slow-growing bacteria, which are able to degrade organic matter. The evidences for the effectiveness of expanding the SRT for MBR operation are inconsistent. There is no indication that the treatment of pathogenic microorganisms like viruses has been improved [36];[37]. This is understandable, considering that particle exclusion is unaffected by reactor particle concentration. However, there is conflicting knowledge on dissolved organic and inorganic compounds. Micropollutants are small particles that pollute the environment; elimination of these dissolved species isn't achieved explicitly,

since they have molecular weight smaller than the membrane cut off so they are usually removed by Degradation or phase change. Volatilization (aided by aeration, i.e. sparging), adsorption into sludge, or precipitation are all ways to phase change. Organic micropollutants have the ability to degrade and, as a result, solids and liquid retention time in the bioreactor can have an effect on the treatment mechanism of these Organic micropollutants. The latest research of the literature on the subject of PPCP. [38] has found that:

- Pharmaceuticals that are easily eliminated (acetaminophen, ibuprofen, and, paroxetine) are removed relatively well in all the ASPs and MBRs.
- For some moderately eliminated products (sotalol and hydrochlorothiazide) as well as extremely refractory products like (carbamazepine) [39], There is no significant difference in their removing efficiency between the MBR, and ASP, generally, these species are currently induced by biotreatment through diverse physico-biochemical processes.

- The elimination of most other PPCPs seems, but does not significantly, to be better for the MBR over that of an ASP to exclude many pharmaceutical products [40];[41].

Important improvements in recalcitrant low biodegradable polar contaminants, such as diclofenac, mecoprop, and sulfophenylcarboxylates, have nevertheless been recorded [39]. Studies carried out at very long SRTs and in proportion to the low F/M ratios have provided greater eliminations for some PPCPs [42]. Studies showed comparable efficiencies for CASPs and MBRs for specific types while both systems were performed with the same SRT [41]. Several researchers did not find a direct relation between SRT and PPCPs biodegradation. [43]; [44];[45]; since for some compounds such as diclofenac [46] There tend to be significant other operating parameters; little more removing at SRTs exceeding 30 days is achieved [47]. While this related highly fluctuating loads showed a comparable output of decentralized plants to that of larger centralized systems[48]. so that, if the design of the reactor is plug-flow, their percentage removal would depend heavily on residence time, not on concentration. This seems to have happened with many acidic pharmaceuticals at a lower pH [49]. pH is believed to affect micropollutant elimination according to the acid dissociation pKa value, which would then influence its propensity for the mostly hydrophobic solids [40]. A significant association between PPCPs elimination and nitrification has been identified [50];[51]; Bacteria that nitrifying organic pollutants and enzymes specifically including ammonium monooxygenase[52], have been assumed to be capable of co-metabolizing a broad range of organic recalcitrant micropollutants [53]. Also, indications of the influences of existence or depletion of C and N have shown in terms of substantially higher diclofenac degradation under an anoxic than aerobic environment [54].

2.8 Occurrence of Micropollutants and Their Impact on the Environment

2.8.1 Occurrence of Micropollutants in Wastewater and Surface Water

Table 1 shows the list of micropollutants routinely observed as well as with average wastewater and surface water concentrations. Various factors like production rate, average sales, and use, water use per capita/day and level of excretion, and seasonal changes can influence the accumulation of such compounds in wastewater [55]. The production and use of micropollutant components also specify the amount of micropollutants in the WWTP [56].

2.8.2 Occurrence of Micropollutants in Groundwater and Drinking Water

Groundwater pollution with EMPs is mainly occurred by sewage systems, septic tanks, ground-to-surface water penetration by soil, permeation of landfill leachate and, drainage of agricultural lands' polluted water. The amount of EMPs in ground water relative to that in the surface was found to be less [57]. Triclosan, sulfamethoxazole, carbamazepine, and non-steroidal antiinflammatory medications are the most frequently found in groundwater micropollutants. These residues are also common in surface water and waste water, confirming a correlation in different water bodies with micropollutants [58].

2.8.3 Impact of Micropollutants on The Environment

Because of their bioaccumulative and non-biodegradable existence, many micropollutants are deemed highly harmful to ecosystems, like aquatic life (leading to genotoxic, estrogenic, and mutagenic effects), wild animals, and humans. Take,

Table 2.1 Micropollutants Commonly Found in Domestic Wastewater and Surface Water [59], [60]

Pharmaceuticals	Application	Average concentration in surface water (ng/L)	Average concentration in wastewater (ng/L)
Carbamazepine	Antiepileptic	110	832
Acetaminophen (paracetamol)	Therapeutic	250	10194
Diclofenac (Sodium Salt)	Anti - inflammatory	65	647
Ranitidine Hydrochloride	Anti-histamine	10	188
Atenolol	β-Blockers	205	843

for example, the feminizing of male fish caused by exposing to endocrine disrupting compounds (EDCs) [59]. Also at trace concentrations, the continuous release of EDCs into the environment causes genotoxicity and developmental defects in highly susceptible animals. Furthermore, the enhancement of antibiotic-resistant microorganisms is proving to be a threat. The haphazard and the ever rising use of antibiotics to enhance animal and human health has resulted in antibiotic resistance

genes have evolved in a variety of environment. The amount of micropollutants released into the environment is expected to increase owing to population increase and a heavy dependence on pharmaceuticals, the cost of health care will continue to rise in the future.

2.9 Micropollutant Removal Mechanism Using MBR System

Physical retention by a membrane, air stripping, sorption, biodegradation, and photo-transformation all contribute to the removal of EMPs from wastewater by an MBR process. [47]. Biodegradation is the primary mechanism for polar contaminants, and sorption is really poor [60]. When the molecular weight of the micropollutants is so smaller than the MW cut off of the microfiltration membrane, sorption space is reduced. Micropollutant sorption, on the other hand, happens as a result of the development of a second layer because of the accumulation of micropollutants [61]. Although air stripping/volatilization is used to extract extremely volatile trace organics from wastewater, it is found to be negligible since the bulk of contaminants have a Henry constant of less than 0.005.[62]. Biosorption takes place on activated sludge for hydrophobic pollutants, while biodegradation takes place for hydrophilic pollutants. [63]. Furthermore, the presence of multiple degraded transitional byproducts/metabolites has a bad influence on the biodegradation and sorption removal mechanisms. [64].

2.9.1 Sorption

Pollutants form associations with the solid phase in this phenomenon. Just a small percentage of contaminants are absorbed by the sludge, while the majority remain unaffected. To determine the amount of sorption of micropollutants, the solid water distribution coefficient (Kd) is significant. It plays a crucial role and is characterized as the amount of pollutant present as solid in the environment to the amount in the aqueous phase (at equilibrium) [38]. Equation (2.1) can be used to express the value of Kd (L kg^{-1}) at equilibrium [65].

$$K_d = \frac{(Csorbed)}{(Xss)(Ssoluble)} \quad (2.1)$$

where, *C*sorbed: sorbed compound (μg L^{-1}), *X*ss: concentration of the suspended solid in wastewater (kg L^{-1}) and *Ssoluble*: concentration of the soluble part of the compound (μg L^{-1}). Adsorption (electrostatic interactions of positive groups of micropollutants with the negative surface of microorganisms) and absorption (hydrophobic behaviors of pollutants with the lipophilic membrane of microorganisms and lipid sludge proportions) are the two main mechanisms that cause the pollutant to become sorbed into the primary, and secondary activated sludge. [38], [40]. Absorption is distinguished by a coefficient of octanol water (Kow) [40]. A low log Kow value also contains information concerning the sorption phenomenon and the hydrophobic nature of contaminants suggesting that the activated sludge is first absorbed the micropollutant, then biodegradation is happened [66].

In most cases, the Kd value in primary sludge is slightly greater than in activated sludge, indicating the inhibition in primary sludge [67].

2.9.2 Biodegradation

Biodegradation is a renowned biological process on which microorganisms degrade micropollutants and redox conditions in the polluted aquatic environment are dependent [40], [68], [69]. It is the most significant phenomenon in MBR with the scope of micropollutants removal and is following the pseudo-first order degradation kinetics (Eq.(2.2)) [70]:D

$$\frac{dC}{dt} = K_{biol} X_{ss} S_{soluble} \quad (2.2)$$

where, C: concentration of the micropollutant (μg L^{-} *Ssoluble* ^{1}), Ssoluble: concentration of the soluble part of the micropollutant (μg L^{-1}), Kbiol: pseudo- first order reaction rate constant (L gss^{-1} day^{-1}) and Xss: concentration of the suspended solid (gss L^{-1}) and t: time (day). Because aerobic conditions are far more desirable to

the microorganisms clusters found within the MBR system, they are also desirable for biodegradation. The acetaminophen removal rate was stated to be more than 80% in the MBR sludge. [71], [72]. Since anti-inflammatory drugs and activated sludge have a similar negative charge, sorption is poor, and biodegradation is the primary mechanism of removal[65]. Besides that, micropollutants such as carbamazepine are refractory pollutants with a low biodegradation rate (less than 20%), making the discharge of such contaminants a threat during the MBR process [73],[74]. MBR systems with a high SRT for diclofenac have since been identified as a reasonable alternative for such cases. [72]. Furthermore, the biodegradation removal rate varies significantly depending on sludge source, age, wastewater composition, microbial community, and aeration [48].

2.9.3 Stripping/Volatilization

Stripping is the process of removing gaseous contaminants from aerobic WWTPs that contain micropollutants. The stripping is primarily determined by the vapor pressure of the wastewater (i.e. Henry's constant (H)) and the hydrophobicity of the wastewater. [60]. Since most micropollutants have a very low H/log Kow value (Kow: octanol water partition coefficient), the phenomenon is negligible. Volatilization is a big deal if H is a high value [40], [75], [76]. Volatilization is negligible for pharmaceuticals [62] because of low H-value and hydrophobicity.

2.10 Factors Affecting the Removal of Micropollutants from Wastewater

The physico-chemical properties of the compounds, as well as operational parameters (biomass concentration, SRT, HRT, temperature, and pH) of the wastewater to be treated, determine the fate of micropollutants during MBR treatment. Sorption and biodegradation are two of the most essential removal processes of micropollutants from wastewater, according to the literature, and both mechanisms are related to the availability of a substrate for degrading microorganisms. [77], [78].

2.10.1 Chemical Properties of Micropollutants

2.10.1.1 Hydrophobicity and Hydrophilicity

The physical property of a compound that is pushed away from a mass of water is known as hydrophobicity. Hydrophobic compounds make up a large portion of the organic micropollutants present in wastewater. The key property that causes sorption to sludge, lipid, and particulate matter throughout wastewater treatment is hydrophobicity. Micropollutants can attach to suspended solids and then be discarded during the wastewater treatment process by removing excess sludge. The Kow ratios, which represent the partitioning equilibrium of the organic solute between the organic phase (octanol) and the aqueous phase (water), can be used to estimate micropollutant sorption to the solid phase. [40]. Hydrophobic materials, low hydrosolubility, and a high propensity to sorb on organic matters in the sludge mixture are all signs of a high Kow. [40]. The sorption to activated sludge is not greatly attributed to the elimination of contaminants through excessive sludge removal for substances with log Kow less than 2.5. Moderate sorption is predicted between log Kow 2.5 and 4 and values greater than 4.0 are compatible with high sorption ability. [40]. Certain pharmaceuticals (e.g. diazepam, diclofenac, ibuprofen, naproxen, sulfamethoxazole) were removed from sewage treatment plants due to absorption of those substances by sludge in the biological reactor (aeration tank) [79]. The sorption was also visible during the primary treatment for fat isolation, with removal rates varying from 20 to 50% due to the lipophilic properties of organic contaminants. Carballa (2005) investigated the behavior of EMPs with much hydrophobicity (galaxolide, tonalide) during various stages of wastewater treatment and matched the findings to those of much polar pharmaceuticals (e.g., ibuprofen, naproxen, diclofenac, diazepam, carbamazepine). Once again, it was determined that the strong sorption characteristics of the investigated hydrophobic matters resulted in up to 70% elimination. On the other hand, there was no evidence of carbamazepine elimination. [10]

2.10.1.2 The Chemical Structure

The chemical structure is another significant property to consider when assessing the removal potential of organic EMPs. The chemical structure and basic composition of a compound may have an effect on the removal rates of wastewater throughout MBR processing. Pharmaceuticals are complicated molecules that are distinguished by their ionic composition. Compounds with a complicated chemical structure, such as ketoprofen and naproxen, were not removed by the CTP system but were by MBR. [80]. The existence of a complex structure with dual aromatic rings, which makes the compound more robust to degradation, is thought to be the cause of weak elimination in CTP. Micropollutants in dual aromatic rings, such as ketoprofen and naproxen, exhibited higher elimination using the MBR method as the SRT increased, attributed to the existence of a varied microbial community that is acclimatized and capable of degrading the aromatic rings. Even though it is hard to relate removal efficiency to compound complexity, it can generally be determined that aliphatic monocyclic aromatic compounds with electron donating groups are easily biodegraded, whereas polycyclic aromatic compounds with electron withdrawing groups are more resistant to degradation. [81], [82]. Tiny molecules with chlorine groups, such as clofibric acid and diclofenac, were not effectively eliminated by both CTP and MBR. As a result, these researchers correlated the micropollutants' resistance to the existence of halogen groups. Nonetheless, this hypothesis needs to be investigated further. The same authors suggested a category of micropollutants into compounds based on their removal degree and chemical structure which are:

- Both CTP and MBR can easily remove it (i.e. ibuprofen and acetaminophen),
- Not effectively eliminated in both systems (i.e. clofibric acid, carbamazepine, diclofenac), and
- CTP failed to eliminate it completely, but MBR did (i.e. ketoprofen, mefenamic acid, and naproxen).

Other researchers claim that the increased quantity of nitro- and chlorine-groups in aromatic chemicals reduces the rate of degradation. [83].

2.10.2 Process Parameters

2.10.2.1 Sludge Retention Time (SRT) and Biomass Concentration

Microorganisms mean residence time in CTP and MBR systems is referred to as sludge retention time (SRT). According to numerous studies, adequate high SRT is needed for the elimination and degradation of micropollutants from wastewater, as well as the enhancement of slowly growing bacteria and the formation of a much more extensive biocoenosis capable of degrading a wide range of micropollutants. Short SRTs (less than 8 days) remove certain bacteria from the process, so biodegradation becomes less important and adsorption to sludge is more important. At SRT greater than 8 days, a diverse microbiocoenosis may grow, like nitrifying bacteria. In oxygenated tanks, endogenous microorganisms arbitrate nitrification, which results in the transformation of ammonia to nitrate. Complete nitrification in MBRs with organic loading rate of 0.05–0.66 kg BOD m^{-3} d^{-1} and sludge age of 5–72 days [84].

Biodegradation is influenced by biomass characteristics, which vary between CTP and MBR treatments. At younger sludge ages, the probability of genetic mutation and microorganisms adaptation to integrate stable organic matters rises. [85]. In addition, those enzyme activities are proportionally increasing to the greater specified area of the MLSS, which is directly linked to the floc structure. The sludge composition differs depending on the influential composition and operational parameters for the treatment of wastewater [85]. For the biotransformation of certain drugs, i.e. bezafibrate, sulfamethoxazole, ibuprofen, and acetylsalicylic acid, SRT values within 5 and 15 days are needed. [86]. However, applying high SRT does not immediately cause all contaminants to be removed. For two days SRT, Clara et al. (2005) [46] showed that nothing was removed, while when SRT was applied 82 days in MBR and 550 days at CTP removal rate was more than 80%, of the pharmaceutical products, for example, ibuprofen, benzothiaseol, and diclofenac. However, the

removal rate for all investigated SRTs of carbamazepine remained under 20% [40]. Ternes et al. have also published the same findings (2004)[65] revealing that even SRT over 20 days is not enough with carbamazepine and diazepam elimination. Diclofenac extraction ranged from 44 to 85% at SRT between 190 and 212 days in MBR with acclimatized biomass. [87]. Biodegradability of identified pharmaceuticals was measured in a lab scale MBR with high sludge concentrations varying between 20 and 30 g/l and an SRT of 37 days. Ibuprofen degradation began after 5 days and was finished after 22 days [88]. Once the SRT was reduced, the lower degradation rates were attributed to the lower biomass concentrations.

2.10.2.2 pH Value

By affecting both the physiology of microorganisms (optimum pH of microbial enzyme activities) and the solubility of micropollutants found in wastewater, the acidity or alkalinity of an aqueous medium may affect the degradation of organic micropollutants existing in wastewater. For example, tetracyclines are uncharged at pH 6–7, so adsorption sludge is becoming a significant removal mechanism. [89]. It was also discovered that norfloxacin's hydrophobicity differs with pH, being very weak at pH 4 and very high at pH > 10, with the maximum hydrophobic value being obtained at pH 7.5. A further study established pH as an important parameter influencing micropollutant elimination throughout MBR processing. With pH ranging from neutral to acidic nitrification becomes more important in the MBR. Ibuprofen was considered to have a significant elimination efficiency (up to 90%) at pH levels less than 6. When the pH fell under 5, ketoprofen was extracted from MBR at the rate of 70%. [40].

2.10.2.3 Temperature During Wastewater Treatment

The temperature affects microbial development in both CTP and MBR, as the rate of microbial growth differs widely depending on the ambient temperature. [90]. As temperature increases, adsorption equilibrium is reached sooner, and the rate of degradation and microbial growth accelerates. Removal of pharmaceuticals like

ibuprofen, bezafibrate, diclofenac, naproxen, and ketoprofen improved during summer while the water temperature reached 17° C, compared to that in winter when the water temperature was about 7° C. [91]. The degradation rates decreased as the temperature dropped during the winter. When it comes to diclofenac, naproxen, and ibuprofen, systems that are run at 25°C perform better than those that are run at 12°C. [79]. Another research compared the elimination of pharmaceuticals (phenazone, carbamazepine, and metabolites) during the CTP and MBR processes and found that the CTP process' output maintained fairly stable over time despite seasonal temperature changes (10–25C), whereas the MBR process' biodegradation rate was heavily influenced by temperature variation [92]. The increase in temperature in the MBR during the summer, as well as the long sludge age (26 days), raised the removal rates to 80–100 %. According to the same research, pharmaceuticals were removed up to 99 % in MBR units, and steroids were removed up to 80 % in MBR units in the summer. The temperature affects the adsorption of antibiotics fluoroquinolone to the particles in raw water. Researchers have investigated the impact of high temperature on COD removing from pharmaceutical industry wastewater came to the fact that temperature acts as a positive selection for the growth of bacterial communities under aerobic biological wastewater treatment. [93]. Simultaneously, it encourages pharmaceuticals to degrade at a faster rate.

2.10.2.4 Effect of Redox Condition

The MBR is performed under a variety of redox conditions, resulting in a high microbial diversity and behavior. Suarez et al. [94] Certain micropollutants (naproxen, 17-ethynylestradiol, and ibuprofen) biodegraded significantly during aerobic conditions, whereas others did not. Galaxolide and tonalide, under both aerobic and anoxic environments, they can be degraded. Anoxic environments have been shown to be able of removing micropollutants from wastewater in several studies. [95]. For example, the diuron removal efficiency was accomplished at 95% under anoxic conditions compared to only 60% under aerobic conditions. [94].

Micropollutants including gemfibrozil, diclofenac, bezafibrate, and ketoprofen were partially removed by nitrification. A higher SRT in an MBR technology allows for the enhancement of nitrifying bacteria, resulting in removing such trace micropollutants [96].

2.11 Emerging Micropollutants Removal Mechanism by Combined MBR-NF/RO Treatment System

The only way to minimize the environmental and health problems correlated with the reclamation and reuse of water is to handle it properly. The type of treatment is determined by several variables, including recycled water uses and treatment efficiency, wastewater characteristics, the existence of certain organic compounds, compatibility with established conditions, needed adaptability, skilled personnel availability, energy requirements, chemicals, and the presence of environmental restrictions [97]. As earlier highlighted, conventional activated sludge technologies are often insufficient to achieve higher degradation rates for most organic micropollutants. As a result, various alternative technologies have been investigated, including hybrid methods, which are a mixture of two or more treatment processes and may seem to be successful in removing micropollutants. Because of synergistic effects, the removal of certain refractory contaminants can be enhanced by combining two methods. Despite the fact that microfiltration (MF) and ultrafiltration (UF) are established processes for removing turbidity, some micropollutants are typically improperly extracted during UF and MF because membrane MW cut off are much bigger than micropollutant molecular sizes. As a result, post-treatment processes are necessary to gain high water quality. Because of experimental difficulties for detecting and quantifying EMPs in the trace levels that exist in aquatic environments, the analysis of EMPs is complicated. Furthermore, variations in the methodological approaches used for their analysis have been identified in the literature [98]. In spite of the fact that several research pointed to their long-term effects, there are no regulations on the large majority of these pollutants. One of the most distinguishing

features of EMPs is their high rate of production and human use, resulting in continuous feeding into the environment. EMPs have been described as a major environmental health issue in treated wastewater [56]. Aquatic toxicity, endocrine destruction, genotoxicity, and strengthened pathogenic bacteria tolerance are some of the bad consequences [99]. Many EMPs have been found in various water matrices, according to the publications [100], [101]. Even so, the effect of low concentrations of these contaminants in water sources on the environment and human health is unclear [102].

NF and RO membranes are two of the most effective applications for EMP elimination [103], [104]. Most of those EMPs that exist in the system can be almost fully removed using NF and RO membranes. While NF membranes use less energy than RO membranes, several other energy-saving RO membranes achieve large flow rates with low pressure. EMP elimination has only been studied in a few researches using the combination treatments MBR–NF or MBR–RO. Furthermore, the majority of reported studies used synthetic wastewater and were conducted in a lab setting. As a result, the research community faces a new challenge in terms of new approaches incorporating various technologies to increase EMP removal efficiencies, as well as for full-scale experiments with real wastewater. Nanofiltration membranes (NFs), that have super preservation for multivalent ions and organic compounds at low operational pressure, have gotten much interest in the wastewater treatment and reclamation field in current years. COD and colored elements can be completely eliminated from biological wastewater treatment effluent using NF membranes [105]. RO and NF membranes are effective barriers for contaminant preservation and can efficiently remove target pollutants [106]. Due to the benefits of MBR and RO/NF, double membrane systems combining MBR and RO or NF have lately gained popularity as a promising and effective treatment option for the extraction of trace organic contaminants or wastewater reuse. [107], [108].

Removal efficiencies in RO are influenced by three factors: (a) Membrane characteristics (molecular weight cut off, porosity, morphology, charge, and hydrophobicity); (b) molecular characteristics (molecular weight, molecular structure, charge, solubility, and hydrophobicity); and (c) context fluid characteristics (pH, alkalinity, and the amounts of other organic and inorganic contents) [109]. These properties have three key mechanisms that influence removal: (1) size exclusion based on molecule diameter and width; (2) hydrophobic adsorption as measured by solubility and the octanol–water partitioning coefficient (Log Kow); (3) molecule solubility and electrostatic repulsion/attraction, which are affected by molecule charge and acidity, as measured by the acid dissociation constant (pKa) [110]. An RO membrane's nominal pore size is less than 0.5 nm, allowing it to remove not only bacteria, viruses, humic compounds, and colloids (as used in UF membranes with nominal pore sizes of 1.5–60 nm), but also molecules and ions. [111]. Because most OMPs have molecular weights greater than 200 g/mole, size exclusion is found to be the major mechanism of elimination. In addition to size exclusion, hydrophobic interactions can cause the sorption of relatively nonpolar substances to the membrane surface [112], [113]. Garcia et al. [114] for domestic wastewater reuse, MF and RO were combined to eliminate micropollutants. The removal efficiency of most micropollutants was substantially improved with the addition of RO, ranging from 65% to 90 % (except ibuprofen and nonylphenol). Likewise, except for mefenamic acid and caffeine, a tertiary MF/RO treatment procedure showed very effective retention (>95%) of most of the investigated pharmaceuticals [115]. Nanofiltration (NF) and reverse osmosis (RO) have much "tighter" structures than MF and UF. Because of their high contaminant removal performance, NF and RO are widely used in the water reuse industry. Nevertheless, some comparatively small micropollutants can still pass through NF and RO membranes. [116]. Röhricht et al. [117] for the elimination of pharmaceutical products from WWTP effluent, two separate forms of immersed NF flat sheet modules were examined. When compared to carbamazepine (slight removal), naproxen and

diclofenac (60%) were rejected to a higher degree. Naproxen and diclofenac (pKa = 4.2 and 4.15, respectively) were deprotonated at pH 7 and 8, but carbamazepine (pKa = 13.9) was not. As a result, the negatively charged membrane surface could retain naproxen and diclofenac, but carbamazepine could not be eliminated. This was in line with Schäfer et al. point of view. [118] and Nghiem et al. [119]: Pharmaceutical speciation can lead to a substantial change in exclusion as a function of pH, with ionized, negatively charged pharmaceuticals retaining much more. The fundamental physicochemical properties of pharmaceutical molecules play an important role in their preservation, especially for uncharged pharmaceuticals. Adsorption, in addition to electrostatic repulsion, can be used as an essential removal method in some situations. RO has a lot of potential for removing micropollutants, either partially or completely. Sahar et al. [120] used RO after the CAS-UF and MBR processes to see how effective it was at removing micropollutants. CAS-UF/RO and MBR/RO had identical and strong removal efficiencies: >99 percent for macrolides, pharmaceuticals, and cholesterol, 95% for diclofenac, 97% for sulfamethoxazole, and >93 percent for both sulfamethazine and trimethoprim. Despite the highly successful RO application, ibuprofen, diclofenac, salicylic acid, and cholesterol residues of 28–223 ng/L were found in the permeates from both units. This showed that RO was not an absolute barrier to micropollutants, and that supportive treatment methods should be regarded to help RO reach full micropollutant removal. Yangali-Quintanilla et al. [121] NF and RO were used to evaluate the elimination of different micropollutants (pharmaceuticals, pesticides, endocrine disruptors, and others). NF membranes had a removal efficiency that was very similar to that of RO membranes. Tight NF had an average removal efficiency of 82% for neutral pollutants and 97% for ionic pollutants, while RO had an average retention efficiency of 85% for neutral pollutants and 99% for ionic pollutants.

3

MATERIALS AND METHODS

3.1 Design and Operation of the MBR System

The reactor was constructed according to the design and configuration for the size and dimensions of the membrane modules equipped with two PES (polyethersulfone) membranes with 0.45 μm and 0.20 μm pore size (Sterlitech Cooperation, Kent, WA, USA). The aerobic membrane bioreactor was made of a plexiglass material with a cylindrical shape of 17.5 cm diameter corresponding to an 8 L volume and an active operating volume of 4 L. The peristaltic pumps were used to provide pressure for maintaining constant permeate flux and for automatic inoculation of the reactor feed (Shenchen Cooperation, Baoding, China). A level sensor was used to balance the water level of the reactor (Tin Muhendislik, Istanbul, Turkey). The reactor's oxygen demand was provided by ambient air through the air pumps and diffusers. Details of the reactor configuration are illustrated in Figure 3.1.

The aerobic submerged membrane bioreactor (AeSMBR) was fed with synthetic domestic wastewater prepared according to the following recipe: 50 $mg \cdot L^{-1}$ NH4CI, 0.04 $mg \cdot L^{-1}$ MnCI2·4H2O, 0.132 $mg \cdot L^{-1}$ ZnCl2, 4.5 $mg \cdot L^{-1}$ K2HPO4, 4.2 $mg \cdot L^{-1}$ KH2PO4, 0.2 $mg \cdot L^{-1}$ Na2SO3·5H2O, 0.1 $mg \cdot L^{-1}$ CuCl2·2H2O, 2 $mg \cdot L^{-1}$ FeCl3·6H2O, 0.1 $mg \cdot L^{-1}$ NiCl2·6H2O, 0.03 $mg \cdot L^{-1}$ CoCl2·6H2O, 4.4 $mg \cdot L^{-1}$ CaCl2·2H2O, 12.2 $mg \cdot L^{-1}$ MgSO4·7H2O, and 40 $mg \cdot L^{-1}$ peptone. To obtain a 750 $mg \cdot L^{-1}$ concentration of COD, glucose was added.

The membrane tank was equipped with two polyethersulfone (PES) submerged flat sheet microfiltration membranes, one with a pore size of 0.45 μm and the other one with 0.20 μm, respectively. As shown in Figure 3.2, each membrane module is made

of 12 ×12 cm Plexiglas, with a working volume of 217 ml and an active surface area of 56.25 cm2 (7.5 × 7.5 cm).

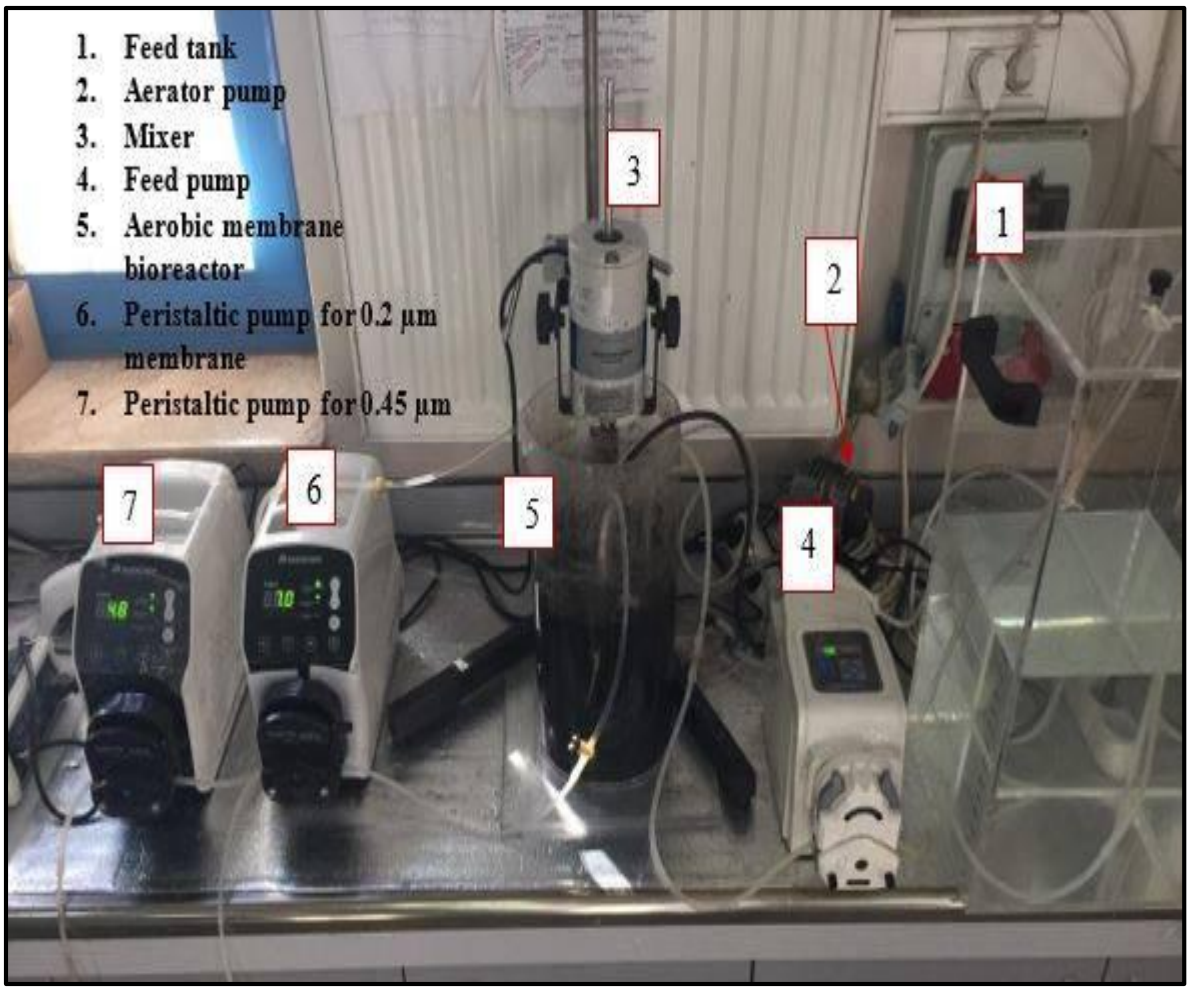


Figure 3.1 Lab-scale set up for submerged membrane bioreactor

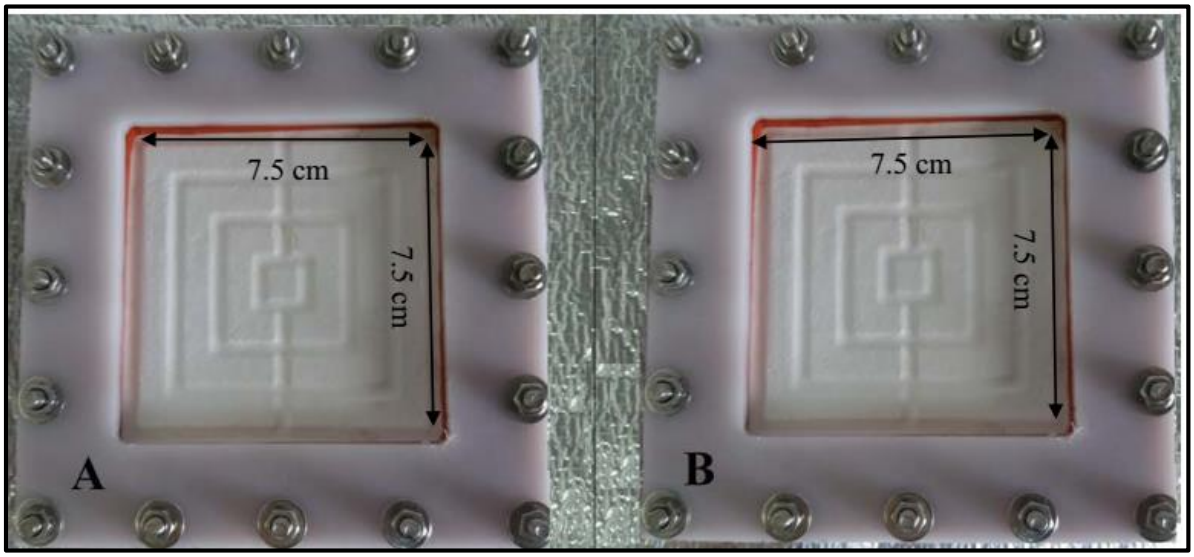


Figure 3.2 module for 0.45 μm membrane (A) and 0.20 μm membrane (B)

3.2 Net Flux

As defined in fluid mechanics, flux is the volume of a fluid passing through a unit area at a specific time. In this context, flux can be formulated as:

$$J = \frac{(Volume)}{(Time\ x\ Area)} \tag{3.1}$$

To provide adequate relaxation time for the membrane, the reactor was operated for 4.5 minutes and stopped for 30 seconds. In this respect, the flux value needs to be recalculated by considering the relaxation time so that the Net flux calculations can rearrange as below:

$$Net\ Flux = \frac{Flux\ x\ Running\ Time}{Waiting\ time + Running\ Time} = \frac{11.11\ x\ 4.5\ min}{(0.5 + 4.5) min} \cong 10\ LMH \tag{3.2}$$

3.3 Samples Preparation

Because of their prevalence, ubiquity, and high human intake in the aquatic environment worldwide target pharmaceutical compounds have been chosen. Target compounds are categorized as shown in Table 3.1 according to their therapeutic effect and physicochemical properties.

High purity grade pharmaceuticals (>98%) were used in this work. Diclofenac, acetaminophen, bezafibrate, carbamazepine, ranitidine hydrochloride, and atenolol were purchased from (Alfa Aesar, Kandel, Germany). The method developed consists of one extraction step for all studied pharmaceuticals, which greatly simplifies the preparation of samples. Individual standard stock solutions in ethanol were prepared based on weight and stored at -2°C. An acceptable dilution of individual stock solutions was established for a mixture of all pharmaceuticals.

According to the literature review [122], [123] the concentrations of this study analytes was chosen as 12 μg/L carbamazepine, 20 μg/L diclofenac, 20 μg/L atenolol, 20 μg/L ranitidine hydrochloride, 12 μg/L bezafibrate, and 100 μg/L acetaminophen (paracetamol).

3.4 Solid Phase Extraction Method

Developed, optimized, and validated technique has been performed followed by liquid chromatography mass spectrometry (LC-MS-MS) for the simultaneous identification of 6 multi-class pharmaceuticals using offline SPE. The SPE method has been developed inspired by literature [124]. For conditioning applications, acetone (HPLC grade), methanol (HPLC Grade), and ultrapure water were used (Merck, Istanbul, Turkey). Table 3.2 shows the conditions that have been applied, including conditioning, percolation, washing, drying, and elution.

To concentrate samples, these compounds were extracted via cartridges given in Table 3.2 by using SPE manifold system equipped with a vacuum pump. To optimize the extraction approach, the efficiencies of various SPE cartridge materials (Oasis

HLB (200 mg, 6 mL) from Waters Corporation and C18 (500 mg, 6 mL) from Agilent) were compared. The detailed procedure was summarized in Table 2, firstly, SPE cartridges for samples 1 and 3 were conditioned with 5 mL MeOH and followed by 5 mL distilled water at a flow rate of l mL/min. The same procedure was applied for the conditioning of SPE cartridges for samples 2, and 4 proceeded with 5 mL of acetone. The water samples were percolated by the cartridges following the conditioning stage. The cartridge was then washed with 5 mL HPLC-grade water and dried for 15 minutes by using a vacuum to extract the excess water. Elution of 2×4 mL of methanol was performed. For direct testing by LC-MS-MS analysis, the extract is reconstituted with 1mL after being vaporized under a moderate stream of nitrogen.

Table 3.1 Main characteristics of selected, analyzed pharmaceuticals [125], [126]

	Carbamazepine	Acetaminophen (Paracetamol)	Diclofenac (sodium salt)	Bezafibrate	Ranitidine hydrochloride	Atenolol
Applications	Antiepileptic	Therapeutic	Anti-inflammatory	Lipid regulator	Anti -Histamine	β-Blockers
CAS Number	298-46-4	103-90-2	15307-86-5	41859-67-0	66357-59-3	29122-68-7
Formula	$C_{15}H_{12}N_2O$	$C_8H_9NO_2$	$C_{14}H_{10}Cl_2NNaO_2$	$C_{19}H_{20}ClNO_4$	$C_{13}H_{22}N_4O_3S.HCl$	$C_{14}H_{22}N_2O_3$
Log K_{ow}	2.45	0.46	4.51	4.25	0.27	0.16
pK_a	13.9	9.4	4.15	3.61	8	9.6
Log D	1.89	0.47	1.77	-0.93	– 0.63	–2.09

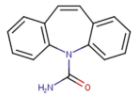
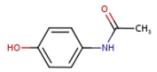
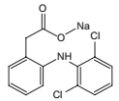
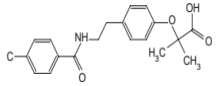
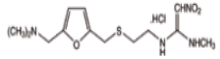
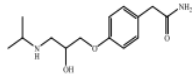
Henry Constant (atm-m^3/mole)	1.1×10^{-12}	6.42×10^{-13}	4.7×10^{-12}	2.12×10^{-15}	3.42×10^{-15}	1.37×10^{-18}
M.W.	236.27	151.17	318.14	361.82	350.86	266.34
Molecular Structure						

Table 3.2 SPE method determination

Applications	SPE Method 1	SPE Method 2	SPE Method 3	SPE Method 4
Types of cartridge	Oasis HLB cartridge 200 mg, 6 mL	Oasis HLB cartridge 200 mg, 6 mL	C18 cartridge, 500 mg, 6 mL	C18 cartridge, 500 mg, 6 mL
Conditioning	5mL MeOH 5mL water	5mL Acetone 5 mL MeOH 5mL water	5mL MeOH 5mL water	5mL Acetone 5 mL MeOH 5mL water
Percolation	100 mL	100 mL	100 mL	100 mL
Washing	5mL Water	5mL Water	5mL Water	5mL Water
Drying	15 min.	15 min.	15 min.	15 min.
Elution	8 mL MeOH	8 mL MeOH	8 mL MeOH	8 mL MeOH

3.5 Analytical Methods

Wet analyses were used to monitor the characterization of the feed wastewater and reactor performance. For the suspended solid (TSS) parameter, standard methods (APHA, 1998) were used [125].

3.5.1 COD Analysis

One of the most crucial parameters in evaluating the strength of pollutants in wastewaters is COD. The COD test was conducted in this research using the inlet feed line and the 0.45 m membrane, with the sample coming from the 0.20 m membrane's exit line. The permeate discharged from the membranes was used in the test without

dilution, and the samples taken from the inlet feed line were diluted 2-fold. As a result, COD analyses have been achieved according to the usual procedures, which included micro-digestion and titration. [126] .

For the test, four COD test tubes were set aside, 2.5 mL of distilled water was used as the blank sample, 2.5 ml of membrane effluent samples were collected, and 1.25 ml of synthetic feed wastewater was taken and diluted 2-fold with 1.25 ml of distilled water before being deposited in COD tubes. As illustrated in Figure 3.4, 1.5 mL potassium dichromate solution and 3.5 mL silver sulphuric acid solution was added to each test tube, which was then capped and placed in the thermoreactor, which had already been adjusted to 150 °C, for 120 minutes. Figure 3.3 shows a WTW CR 3200 thermoreactor.

The tubes were removed from the thermoreactor after 120 minutes and placed near a window for temperature reduction. The beaker is put on the stirrer in Figure 3.3 for titration, and the magnet is thrown in. The COD tubes are emptied into the beaker, and the tubes' insides are cleansed with distilled water before being poured into the beaker. Then, while mixing the beaker with one hand, three drops of ferroin indicator were introduced into the system. The solution was then titrated with FAS and the consumed amount of FAS solution was recorded.

Figure 3.3 WTW CR 3200 Thermoreactor and WiseStir MSH-20A Magnetic Stirrer

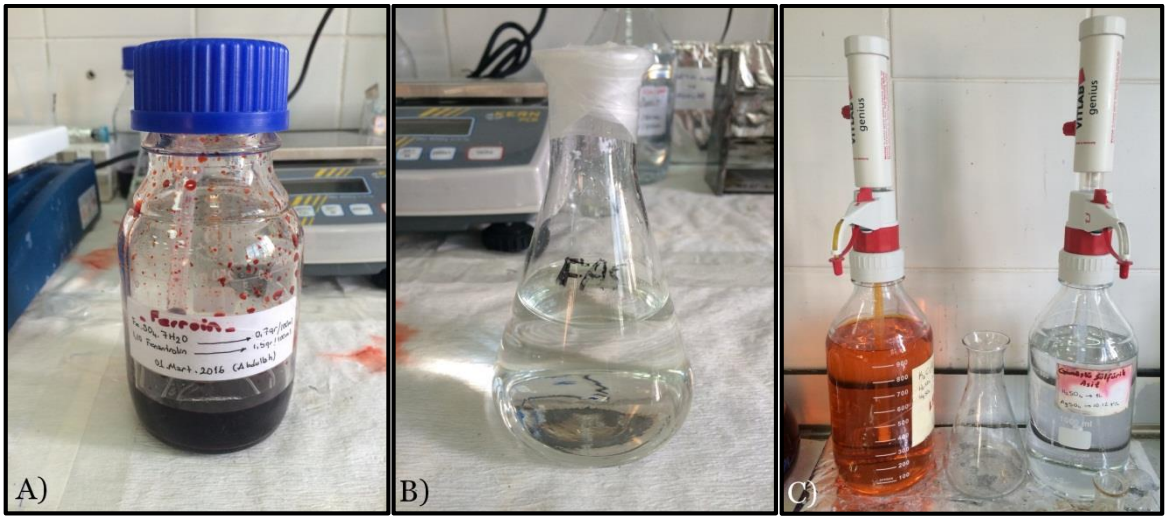


Figure 3.4 Ferroin (A), FAS solution (B), Potassium dichromate and Silver Sulfuric Acid solutions

3.5.2 SMP and EPS Analysis

(EPS) were extracted at 80 ºC for 1 hour using heat treatment [1]. The sample was centrifuged for 10 minutes at 4000 rpm after heat extraction and then filtered by a 0.45 µm filter. The same approach was also utilized for (SMP) samples without heat treatment. Total EPS and SMP were identified by protein and carbohydrate quantifying in the obtained extracts. Bradford[127] and Dubois[128] methods, were used to perform Protein and carbohydrate analyzes respectively. The standards of Bovine Serum Albumin and d-glucose in protein and polysaccharide tests were correspondingly utilized.

3.5.3 TMP Monitoring

Daily pressure readings were taken using the TMP manometer throughout the study. Physical or chemical wash was used when the microfiltration membrane pressure approached 300-350 mbar. The pressure increment suggests that the membrane is becoming clogged. All pressure readings were taken using Installer Logger5 software and a programmable digital manometer which is shown in Figure 3.5.

Figure 3.5 TMP measurement instrument

3.5.4 LC-MS/MS Analyses

HPLC (Shimadzu) equipped with a DAD detector and LC-QTOF-MS/MS (Agilent 6530 Accurate Mass – ESI interface, CA, USA) was used for liquid chromatography analysis. To achieve the chromatographic separation, the Purospher Star RP-18 column (125 mm×2.0 mm, particle size 5μm) is supplied with a C18 guard column by Merck (Darmstadt, Germany). The analyses were performed in Positive Ionisation mode with eluent A (acetonitrile–methanol (2:1)) and eluent B (ammonium acetate 5mM at pH 4.7 (acetic acid)). The flow rate was chosen as 0.3 mL/min, and the injection volume was determined as 10μL. According to the selected method, the eluent gradient started from 5% and rose to 95% of eluent A in 5 minutes (held for 4 minutes), and turned to the initial condition in 5 minutes.

3.5.5 Metagenomic Analysis

Biomass samples at the beginning of the steady state of 40-day SRT (before adding pharmaceuticals) and at the end of 40-day SRT (after adding pharmaceuticals) in aerobic membrane bioreactor were collected and stored immediately at -4°C to measure the percentage of the microbial community. The samples were processed and analyzed as explained below.

3.5.5.1 DNA Isolation

The samples with an amount of 200 mg were transferred to tubes containing 0.1 mm diameter glass beads and 300 μL of lysis buffer (200 mM Tris-HCl, pH 8.0; 20 mM EDTA; 10% TritonX-100) and homogenized for 1 minute at 6000 rpm. In the sample transferred to the new tube to isolate the beads and incubated at the 37°C for 15 minutes, the 10 µL Lysozyme solution (200 µg/µL) was added. Then, 250 μL of lysis buffer (0.5 μg/μL Proteinase K, 5% Tween® 20, 3M Guanidine thiocyanate, 20 mM Tris-HCl, pH 8.0) was added to the sample, incubated for 15 minutes at 70°C, followed by 5 minutes at 95°C. After incubation, 250 μL of 2-propanol was appended to the tube and the sample was loaded onto the silica column. The DNAs in the sample were passed through the silica column by centrifugation at 13000 rpm for 1 minute and kept by the silica column, then were washed twice with wash solution (20 mM NaCl, 2 mM Tris-HCl, pH 8; 80% v/v Ethanol). The silica column was dried by centrifugation. DNAs retained in the silica column were taken from the column with 50 μL of 100 mM Tris-HCl prepared with nuclease-free, sterile, deionized water (pH 7) and preserved at -20°C till doing the analysis. Spectrophotometric methods measured the quantity and consistency of DNA and checked its suitability for the following steps. Other molecular processes were performed using DNAs with an OD260/OD280 ratio of 1.8-2.0, an OD260/OD230 ratio of 2.0-2.2, and at least ten ng/μL (preferably 50-300 ng/μL) concentrations.

3.5.5.2 Next Generation Sequencing (NGS)

The primary pair used to create amplicon libraries that covered about 460 bp region and, the V3-V4 region of the 16S rRNA gene [129]. Connector DNA sequences were added to the 5 ’end of the target-specific primer pairs for compatibility with the Illumina index and sequence adapters of the generated library. The forward primer sequence of the primer-connector oligos specific for 16Sr RNA is 5’TCGTCGGCAGCGTC AGATGT-GTATAAGAGACAGCCTACGGGNGGCWGCAG3’, and the reverse primer sequence is, 5’GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGGACTA CHVGGG TATC TAATCC-3’. The first PCR step was performed using “Bio-Speedy® 2X qPCR Mix” and 200 nm from each primer.

The following thermal cycling program was monitored on the Biorad CFX Connect (Bio-Rad, USA): 3 minutes at 95°C; 25 cycles of 30 seconds at 95°C, 30 seconds at 55°C and 30 seconds at 72°C; 5 minutes at 72°C. By carrying out agarose gel electrophoresis of PCR product size (~550 bp) was confirmed and "Bio-Speedy® PCR Product Cleaning Kit" (Bioeks, Istanbul, Turkey) is used as eluent.

By performing the second PCR step, binary index and Illumina sequencing adapters have been included in the first PCR amplicons by using the Nextera XT Index Kit (Illumina, New York, USA) then, the following program has been used for thermal cycling: 95°C for 3 minutes; 8 cycles of 30 seconds at 95°C, 30 seconds at 55°C and 30 seconds at 72°C; 5 minutes at 72°C. PCR products were cleaned up with a "Bio-Speedy® PCR Product Cleaning Kit" (Bioeks, Istanbul, Turkey). The final library was checked for size (~ 630 bp) by using “Bioanalyzer DNA 1000 chip. To form a library pool, the final library has been diluted to 4 nM using 10 mM Tris pH 8.5 and 5 µL aliquots.

The collected libraries were denatured with NaOH, diluted with hybridization buffer (HT1), and denatured by temperature for batch forming and sequencing preparation, before the MiSeq sequencing. The research was performed using Illumina MiSeq v3

reaction kits. For each reaction as an internal control, a minimum of 5% PhiX has been added.

Usage of Mothur version 1.39.1 to examine unprocessed sequence data (forward and reverse reads merged). The first thing was to cut out the index and main sequences and then classify the particular sequences. The trimmed unique sequences were aligned using the RDP database sequences and the blastn algorithm. Filtering and error checking was done to unaligned sequences at both ends of the sequences. Pollution was prevented by pre-clustering. The UCHIME [130] code was used for the chimera removal. The sequences have been categorized using the Bayesian classifier built into Mothur. With the support of the RDP database, reference and taxonomy files have been gained. Following the operational taxonomic unit (OTU) selection and the taxonomic identification in accordance with the RDP database, OTUs have been categorized in accordance with their phylotypes.

3.6 Membrane Cleaning

Vacuum impact was used across the membrane activities, as well as a steady flux suction and pressure change monitoring were applied. Throughout the vacuum, the TMP device was applied, and the observations were recorded. Membrane pressure was monitored daily with a manometer at each stage of the experiment, and while it approached 300-350 mbar, indicating that the membrane was starting plugged with bacteria and other organisms, physical and chemical cleaning procedures were used. Physical cleaning was used to eliminate surface pollution by gently rubbing the membrane's surface with a sponge and tap water. Only the cake/gel layer was removed from the membrane surface during this rinsing, in an attempt to lower the pressure formed in the membranes and reclaim the flux. Whenever the frequency of membrane blockage rose, chemical cleaning was used. The membranes were cleansed physically using tap water, as detailed above. The membrane was then immersed for one hour in both basic and acidic solutions, with the basic solution being 300 mg/L NaOCl and the acidic solution being 1% (w/v) citric acid. After being well immersed

in tap water, the membranes settled again in the system. New membrane materials were installed in the modules at the end of each experimental phase.

3.7 Experiments of MBR-NF/Ro

MBR permeate has been processed with NF and RO membrane to improve the effluent quality of 0.2 µm and 0.45 µm membrane modules. The SRT of the MBR was maintained within 40 days based on our prior SRT optimization outcomes. Two membrane types of NF and one type of RO membrane were used to examine their efficiency in terms of pharmaceuticals removal. The main characteristics of the membranes used in the experiment were shown in Table 3.3.

In the scope of the analysis, 300 ml of distilled water was first used to wash the membrane before starting the experiment. The water was put over a membrane upon the base of the dead-end Sterlitech brand (P / N HP4750 stirred cell), and the nitrogen (99.95 percent Pure) tube's valves were then released as shown in Figure 3.6. When the washing of the membrane was finished, the MBR permeate filtration process was carried out under a pressure of 10 bar, for the nanofiltration membranes and 15 bar, for the reverse osmosis membrane.

Table 3.3 Characteristics of The Membranes.

SKU	Type	Polymer	Pore size MWCO	Flux (GFD)/PSI
DOW BW30LE	Reverse osmosis	Polyamide-TFC	100 Da	(37-46/225)
FILMTEC NF 90	Nanofiltration	Polyamide-TFC	200-400	(46-60/130)

FILMTEC NF 270	Nanofiltration	Polyamide-TFC	200-400	(72-98/130)

The flux of the FILMTEC NF 270 was 144 ±5 LMH, and the flux of the FILMTEC NF 90 was 83 ±3 LMH, while the flux of the reverse osmosis element was 69 ±3 LMH.

After 30 min of filtration during the experimental period, the permeate was collecting.

For the analysis of systems removal efficiency, effluent samples of both MBRs, 0.2 μm, and 0.45 μm membrane modules, and the permeate of NFs and RO were collected throughout the experimental period three times a week for the evaluation of EMPs removal efficiency. The target samples were preconcentrated using the method of solid phase extraction mentioned before. Then to be submitted for direct testing by LC-MS-MS analysis.

Figure 3.6 The dead-end mechanism (A), the nitrogen tube used in the experiment (B)

4

RESULTS AND DISCUSSION

4.1 Results

4.1.1 Effect of SRT on COD Removal and MLSS Concentration

The bioreactor shown in Figure 3.1 was filled with aerobic activated sludge brought from the Atakoy Wastewater Treatment Plant in Istanbul. The reactor was operated at hydraulic retention time (HRT) (17.7 h), which corresponds to a permeate flux of 10 L/m2·h. During the time to reach the steady-state, the reactor was fed with synthetic domestic wastewater without MPs. After reaching a steady state, the addition of MPs was started. All SRT studies were evaluated separately, and for each of them, the reactor was prepared from the starting point of reaching a steady state case. To evaluate the effect of sludge retention time on COD degradation, pharmaceuticals removal, and bacterial growth, the reactor was controlled for 96 days for each SRT period after reaching steady state conditions. The results of (MLSS), (MLVSS) and, COD are seen in Figures 4.1 and 4.2 respectively.

During the 20-day of SRT, the COD removal efficiency for 0.45 μm membrane was changing between 93.1 – 93.5%, and for 0.20 μm membrane, it was 94.2 – 94.5% (Figure 4.3). In addition, the MLSS values ranged between 5,492 – 5,870 mg/L, and the MLVSS varied between 4,514 – 4,872 mg/L (Figure 4.2). Similarly, at 30 days of SRT, COD removal efficiencies increased slightly (95.6 – 95.9% for 0.45 μm and 96.3 – 96.7% for 0.2 μm membrane), however, MLSS and MLVSS concentrations were 1.5 times higher than the results of 20-day of SRT. Conversely, the increment on COD removal efficiencies was much higher and achieved at 97.3 – 97.7% and 98.0 – 98.2% for 0.45 and 0.2 μm membrane at 40-day of SRT, respectively.

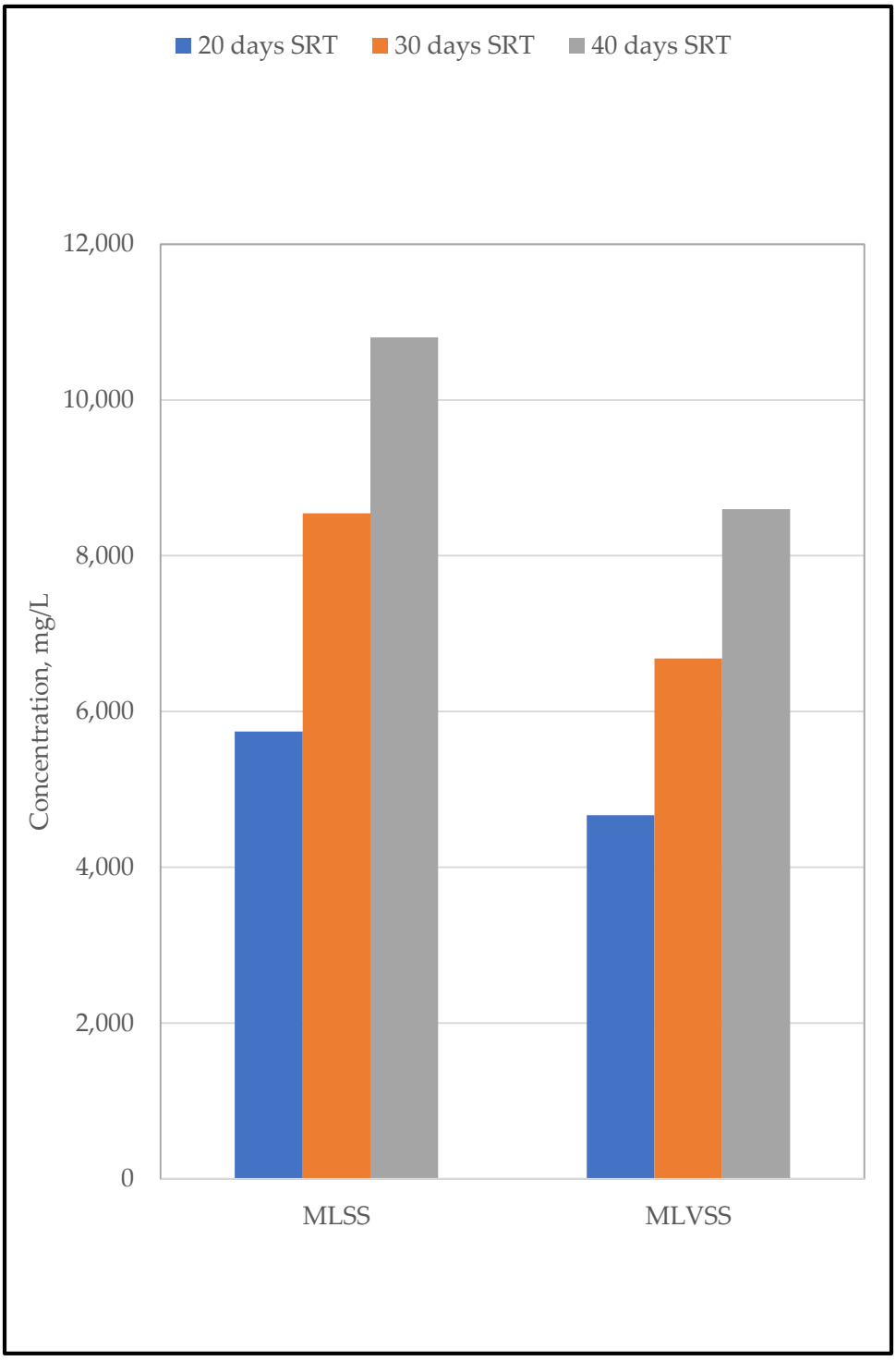


Figure 4.1 The average of MLSS and MLVSS concentrations in different SRT

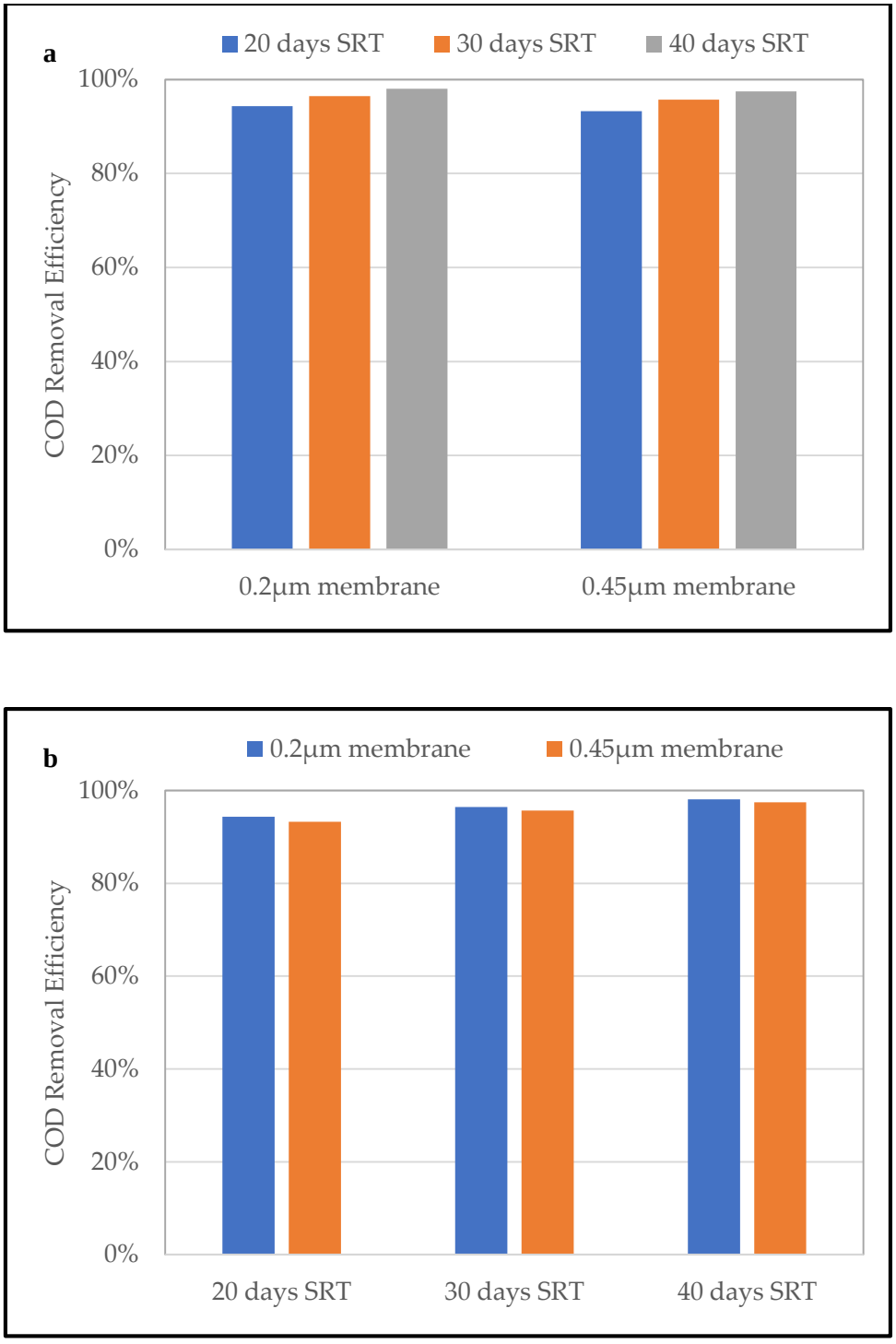
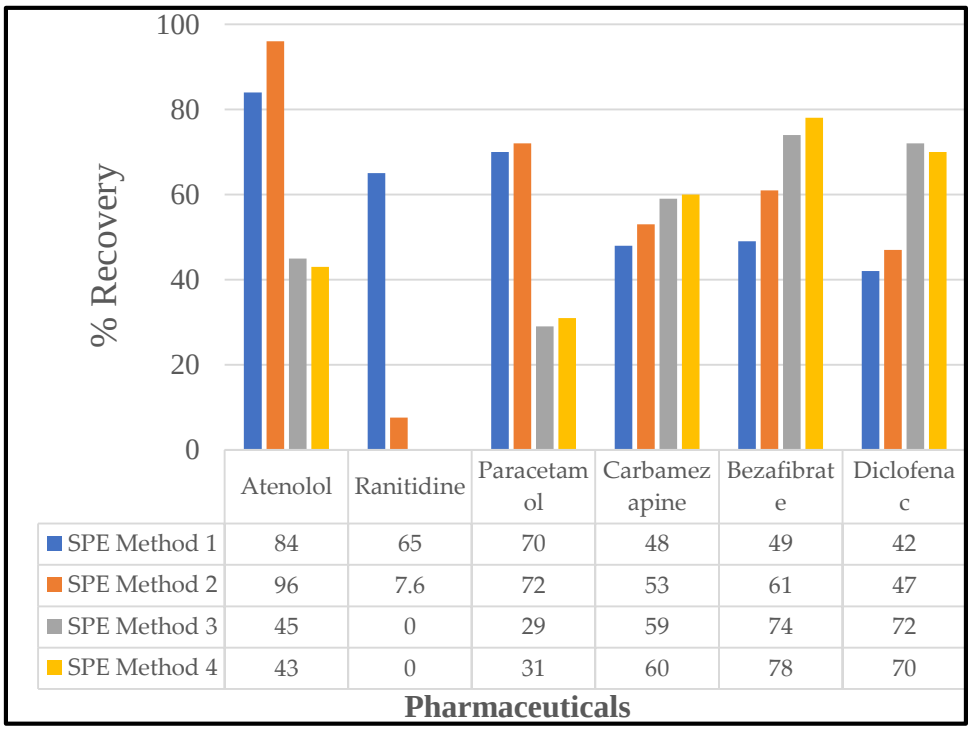


Figure 4.2 COD Removal Efficiency Based on Membrane Type (a), and Different SRT (b)

4.1.2 Determination of SPE Method

To analyze the selected compound by LC/MS-MS, the selected compounds were required to be concentrated by the solid phase extraction method, different solvents and cartridges were compared for their recoveries. The summarized methods were given in Table 3.2. The concentrations of Atenolol, ranitidine, paracetamol, carbamazepine, bezafibrate, diclofenac were 20, 20, 100, 12, 12, and, 20 μg/L, respectively. The volume of the samples used to analyze recoveries was 100 ml. The calculated recoveries can be seen in Figure 4.3.



	Atenolol	Ranitidine	Paracetamol	Carbamezapine	Bezafibrate	Diclofenac
SPE Method 1	84	65	70	48	49	42
SPE Method 2	96	7.6	72	53	61	47
SPE Method 3	45	0	29	59	74	72
SPE Method 4	43	0	31	60	78	70

Figure 4. 3 Recoveries For the Extraction of Selected Pharmaceuticals in Synthetic Wastewater by Using Four Different SPE Methods

4.1.3 Effect of SRT on the Removal of EMPs

During the acclimatization phase, the reactor was supplied with only synthetic domestic wastewater and when the reactor reached steady-state conditions, the mixture of atenolol, ranitidine, paracetamol, carbamazepine, bezafibrate, and diclofenac was pumped with feed pump shown in Figure 3.1. The removal was

monitored for 1 week and the samples were collected accordingly for 20, 30, and 40-day of SRT. The results were given in Table 4.1 in detail, and in Figure 4.4 the removal efficiency was shown for different SRTs through the effluents of 0.2 μm and 0.45 μm membrane equipped MBR system.

According to these results, the 40-day of SRT was selected as the best condition at the steady-state conditions. The concentrations, standard deviations, and LOD, LOQ of studied compounds can be found in Table 4.1, and the comparison of removal efficiencies of all compounds was given in Figure 4.4.

Paracetamol was detected as under the limit of detection at 20, 30, and 40-day of SRT, and according to LOD, paracetamol concentrations were obtained lower than 5.3 μg/L for all conditions. Even the highest concentration within all selected MPs was paracetamol (100 μg/L), the highest removal efficiency was obtained for paracetamol for all SRT. The lowest removal efficiency was observed for carbamazepine for both membranes (approximately 28%) regardless of varying SRTs. This low removal efficiency was also observed by [131]. The diclofenac removal efficiency was observed at approximately 50%, which was comparable to the study achieved by Mousel et al. (2021) [132] studied the UF-MBR process in the degradation of several pharmaceuticals from raw hospital wastewater, found that the removal of anti-inflammatory drugs (ibuprofen and paracetamol) was removed in high efficiencies. If it is desired to sort from the most removed compound to the lowest, it will be Paracetamol, Ranitidine, Atenolol, Bezafibrate, Diclofenac, Carbamazepine for both membranes. These results align with many previous works [133], [134]. It can be concluded that the MBR treatment with several SRT conditions can remove some of the MPs in high removal efficiencies, however, a further treatment process is required for total removal.

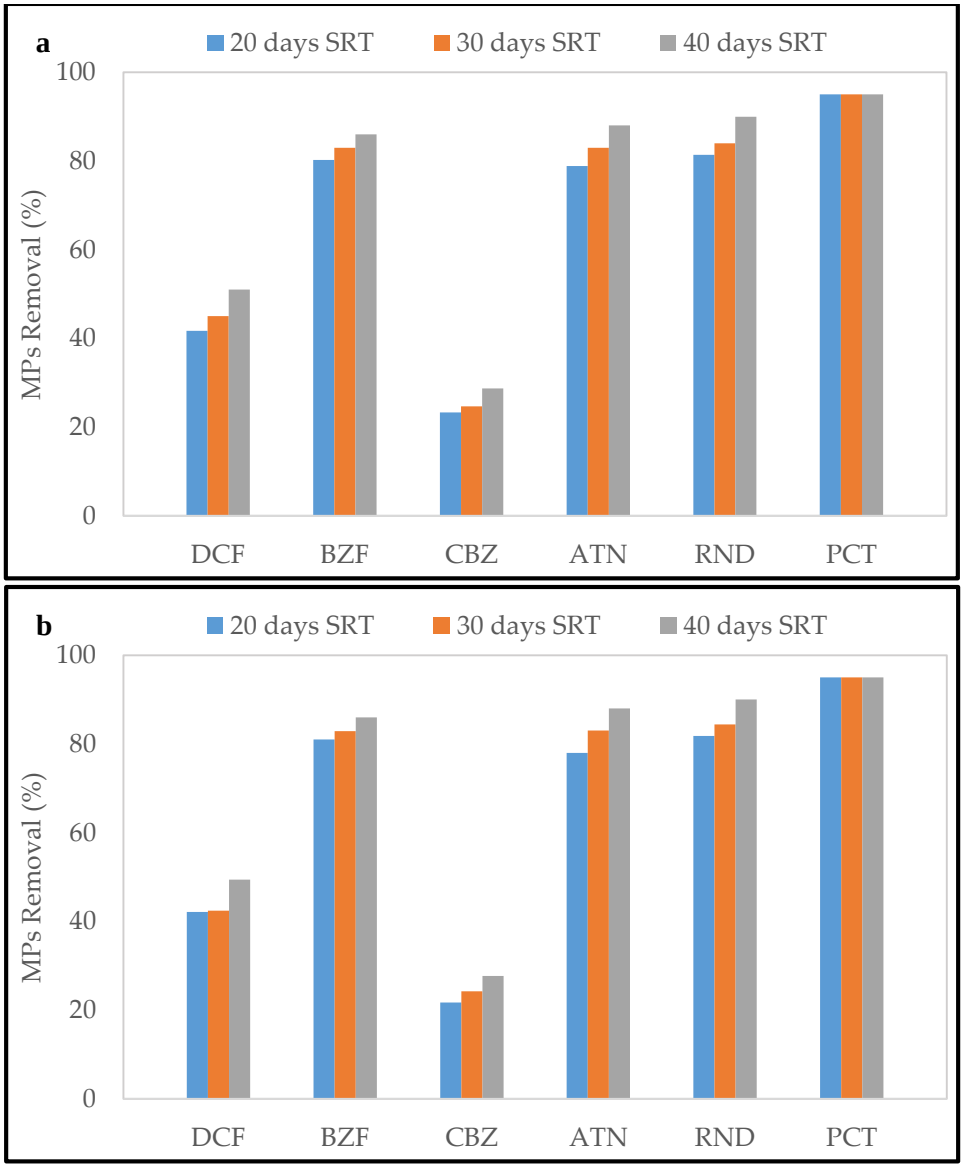


Figure 4.4 MPs removal under different SRT in MBR system equipped with (a) 0.2 and (b) 0.45 μm membrane (DCF: Diclofenac, BZF: Bezafibrate, CBZ: Carbamazepine, ATN: Atenolol, RND: Ranitidine, PCT: Paracetamol)

Table 4.1 The Concentrations in $\mu g/l$ of pharmaceuticals before and after biodegradation

				40-day SRT							30-day SRT							20-day SRT						
Comp.	R^2	LOD	LOQ	Inf.	0.2 µm mem. MBR Eff.	RSD% (n=3)	R.E. %	0.45 µm mem. MBR Eff.	RSD % (n=3)	R.E. %	Inf.	0.2 µm mem. MBR Eff.	RSD % (n=3)	R.E. %	0.45 µm mem. MBR Eff.	RSD % (n=3)	R.E %	Inf.	0.2 µm mem. MBR Eff.	RSD % (n=3)	R.E%	0.45 µm mem. MBR Eff.	RSD % (n=3)	R.E %
DCF	0.997	1.3	4.39	20.76 ± 0.11	10.173 ± 0.19	1.875	51	10.49 ± 0.38	3.713	49.4	20.48 ± 0.34	11.23 ± 0.17	1.496	45	11.8 ± 0.16	1.4	42.4	20.82 ± 0.23	12.13 ± 0.155	1.281	41.7	12.05 ± 0.134	1.112	42.1
BZF	0.997	0.134	0.445	12.48 ± 0.212	1.72 ± 0.012	0.723	86	1.75 ± 0.024	1.4	86	12.44 ± 0.184	2.093 ± 0.005	0.225	83	2.126 ± 0.038	1.814	82.9	12.31 ±. 0.145	2.43 ± 0.011	0.455	80.26	2.34 ± 0.025	0.752	81
CBZ	0.991	1.17	3.9	12.583 ± 0.15	8.96 ± 0.1	1.112	28.7	9.09 ± 0.08	0.933	27.7	12.693 ± 0.15	9.55 ± 0.147	1.539	24.7	9.62 ± 0.237	2.466	24.2	12.428 ± 0.171	9.529 ± 0.085	0.891	23.32	9.731 ± 0.067	0.688	21.7
ATN	0.992	0.64	2.13	20.81 ± 0.12	2.41 ± 0.043	1.79	88	2.51 ± 0.057	2.28	88	20.87 ± 0.042	3.52 ± 0.031	0.877	83	3.5 ± 0.054	1.55	83	20.81 ± 0.262	4.385 ± 0.023	0.522	78.9	4.58 ± 0.037	0.814	78

RND	0.997	0.665	2.22	20.48 ± 0.068	2.02 ± 0.028	1.4	90	2.028 ± 0.049	2.43	90	20.6 ± 0.273	3.28 ± 0.032	0.995	84	3.21 ± 0.088	2.77	84.4	20.52 ± 0.18	3.81 ± 0.008	0.228	81.4	3.73 ± 0.012	0.342	81.8
PCT	0.999	5.3	17.7	103.96 ± 0.81	n.d		≥ 95	n.d		≥ 95	104.033 ± 1.95	n.d		≥ 95	n.d		≥ 95	103.247 ± 1.26	n.d		≥ 95	n.d		≥ 95

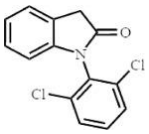
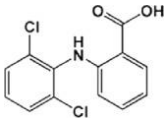
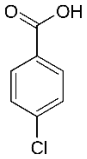
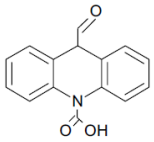
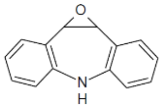
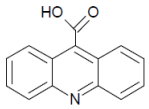
DCF: Diclofenac, BZF: Bezafibrate, CBZ: Carbamazepine, ATN: Atenolol, RND: Ranitidine, PCT: Paracetamol, Inf: Influent, Eff. Effluent, LOD: Limit of Detection, LOQ: Limit of Quantification, RSD: Relative Standard Deviation, R.E.: Removal Efficiency, n.d: not detected.

4.1.4 Removal Mechanisms and Possible Pathways

The presence of possible by-products in the samples of the studies with an SRT period of 40-day and using a 0.2 μm membrane was detected using LC-QTOF-MS/MS. Accordingly, there were no by-products detected for paracetamol, atenolol, and ranitidine. The reason could be the possible by-products could not be concentrated by the method used for SPE. The possible by-products determined for bezafibrate, carbamazepine, and diclofenac were listed in Table 4.2.

As a by-product of Bezafibrate, it is only observed that 4-Chlorobenzoic acid was detected which is the common metabolite for bezafibrate [135]. Furthermore, three possible by-products were determined for Carbamazepine, which is named CBZ-TP1, CBZ-TP2, and CBZ-TP3 as given in Table 4.2. CBZ-TP1 could be formed by oxidation of CBZ molecule (m/z=253). Later CBZ-TP1 could form to lost $-CONH_2$ group and, which is later forming to CBZ-TP2 and CBZ-TP3. Diclofenac compound had also some by-products, which were also observed by activated sludge treatment processes. DCF-TP1 and DCF-TP2 which are DCF-lactam or 1-(2,6-dichlorophenyl)-1,3-dihydro-2H-indol-2-one and DCF-benzoic acid were observed as given in Table 4.2 [136], [137]. Microorganisms have an important function in the transformation of carbamazepine, bezafibrate, and diclofenac by electrochemical reduction and oxidative transformation [138].

Table 4.2 Detected Possible By-products for Diclofenac, Bezafibrate, and Carbamazepine [135], [139]

Transformation Products	m/z	Structure	Formula
Diclofenac			
DCF-TP1 DCF-lactam or 1-(2,6-dichlorophenyl)-1,3-dihydro-2H-indol-2-one	280.095		C14H10NOCl2
DCF-TP2 DCF-benzoic acid	283.036		C13H9Cl2NO2
Bezafibrate			
4-Chlorobenzoic acid	113.05		C7H5ClO2
Carbamazepine			
CBZ-TP1	253.097		C15H12N2O2
CBZ-TP2	210.015		C14H11NO
CBZ-TP3	224.125		C14H9NO2

4.1.5 Bacterial Community Analysis

Inorganic and organic materials are oxidized by microorganisms in oxidation reduction reactions to produce growth and maintenance energy. Under aerobic conditions, electron exchanges (food substrate for an organism) are often part of oxidation reduction reactions and the electron acceptor is oxygen [140], [141].

In this study, the 40-day SRT had the optimum performance in pharmaceuticals elimination and also in COD removal efficiency, so the metagenomic analysis was done for this period to understand the bacterial community before and after adding the pharmaceuticals.

Figure 4.5 shows the percentage of the microbial community at phylum level inoculated in aerobic MBR system of activated sludge and the microbial community percentage for the same conditions at the class level is shown in Figure 4.6 at 0 days during the steady state which is the time before adding the pharmaceuticals and also 96 days after adding the pharmaceuticals. As a result of the metagenomic analysis applied to this sample, a total of 23 phyla, and 58 classes have been identified. Based on 16S rRNA NGS data, the percentage of dominant microbial distributions in raw sludge were found to be 46.8% Proteobacteria, 14.3% Firmicutes, 9.2% Actinobacteria, and 5.4% Bacteroidetes. Proteobacteria represents the predominate heterotrophic bacterial phylum with Gammaproteobacteria, Betaproteobacteria, Deltaproteobacteria, and Alphaproteobacteria classes, the genus of these bacteria were identified to use paracetamol as the sole carbon and energy source [142]. It can be noticed that the Proteobacteria phylum was increased to 60.0% after three months of adding the pharmaceuticals (Figure 4.5) and, especially for the Gammaproteobacteria class it was raised from 25.985% to 44.066% (figure 4.6). Actinobacteria class can metabolize paracetamol, carbamazepine, and atenolol [142] and it was also increased from 9.1% to 17.9% after adding pharmaceuticals.

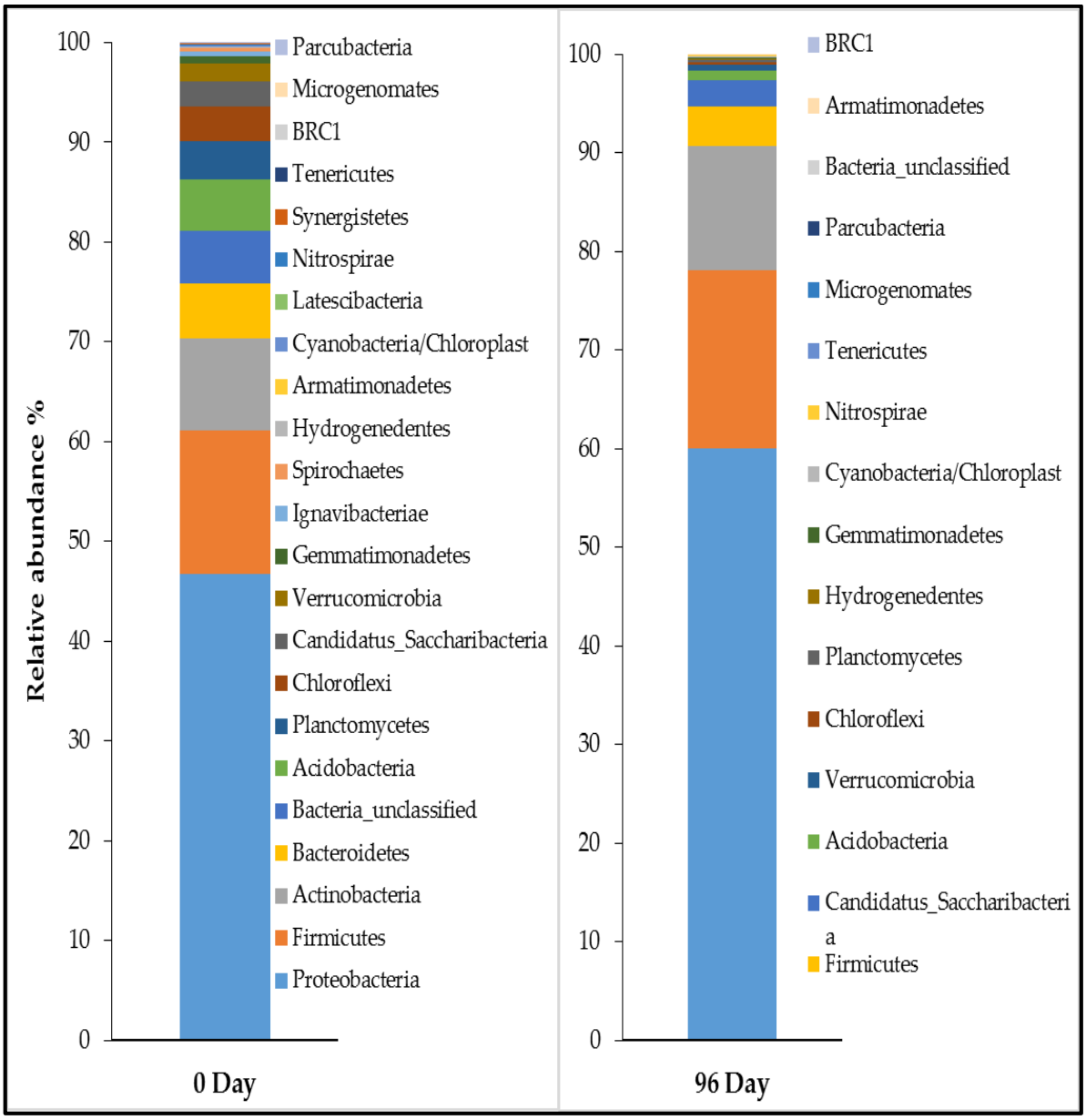


Figure 4. 5 Profiles of Bacterial Community Composition at Phylum Level of Activated Sludge before (at 0 day-left) and, after Adding Pharmaceuticals (at 96 day-right) 40-day SRT

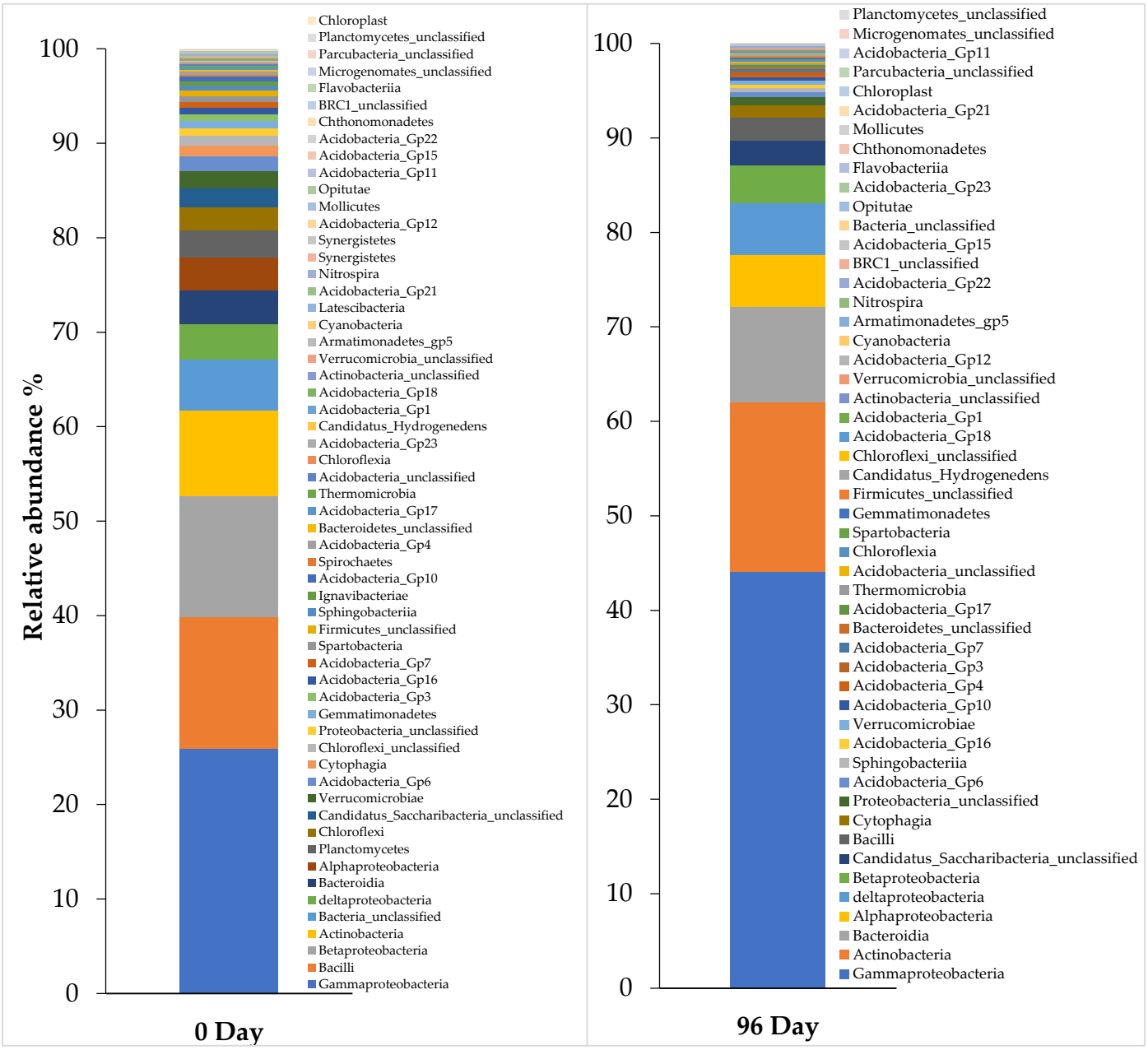


Figure 4.6 Profiles of Bacterial Community Composition at the Class Level of Activated Sludge before (at 0 day-left) and after Adding Pharmaceuticals (at 96 day-right) 40-day SRT

4.1.6 SMP and EPS Results

SMP and EPS analyses were achieved during all the three SRT phases of the experimental study. In MBR, In terms of accumulation and cake formation, SMP and EPS are significant. The extracellular polymeric substance of bacteria, known as EPS, as well as EPS flocs, are generated in the support layer. Many characteristics, such as mud viscosity, sludge resistance, SS, VSS, and SRT, have a direct impact on SMP and EPS values. Because humic acid concentrations in a slurry range from 1% to 4%, several research in the literature report SMP and EPS values as protein and carbohydrate. The different SRT phases were considered in this study, and it was discovered that when the SRT was raised, the SMP and EPS levels declined. The average SMP protein and SMP carbohydrate quantities were determined to be 8.86 mg/gVSS and 22.18 mg/gVSS, respectively, in the 20-day SRT phase of the experimental work. The average protein and carbs quantities were found to be 38.53 mg/gVSS and 56.42 mg/gVSS, respectively, as a result of EPS analysis.

Figures 4.7 and 4.8 show the findings of the SMP and EPS protein and carbs measurements for the three SRT phases in this study. The mean protein and carbohydrate portions were measured to be 6.51 mg/gVSS and 20.62 mg/gVSS in the SMP experiments performed for the 30 day SRT phase of the experimental study The overall average amount of protein and carbs in the EPS, on the other hand, were 34.46 mg/gVSS and 49.16 mg/gVSS, respectively. In the 40 day SRT phase of this work, mean SMP for proteins and carbs were measured as 4.22 mg/gVSS and 17.23 mg/gVSS, respectively, EPS value for protein was found as 31.42 mg/gVSS and for carbohydrate was found as 44.73 mg/gVSS.

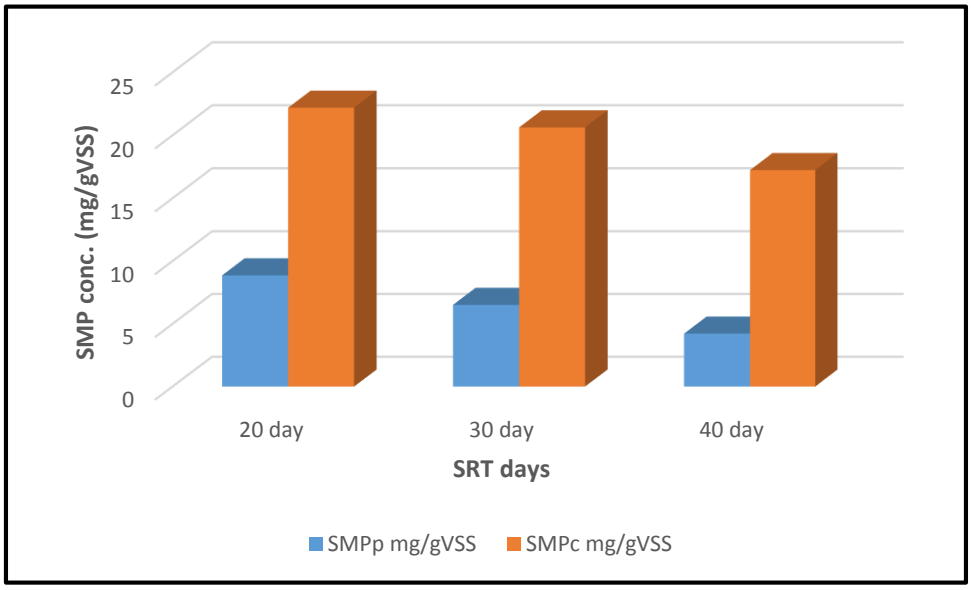


Figure 4. 7 Protein SMP and Carbohydrate SMP of the Reactor Based on Different SRTs

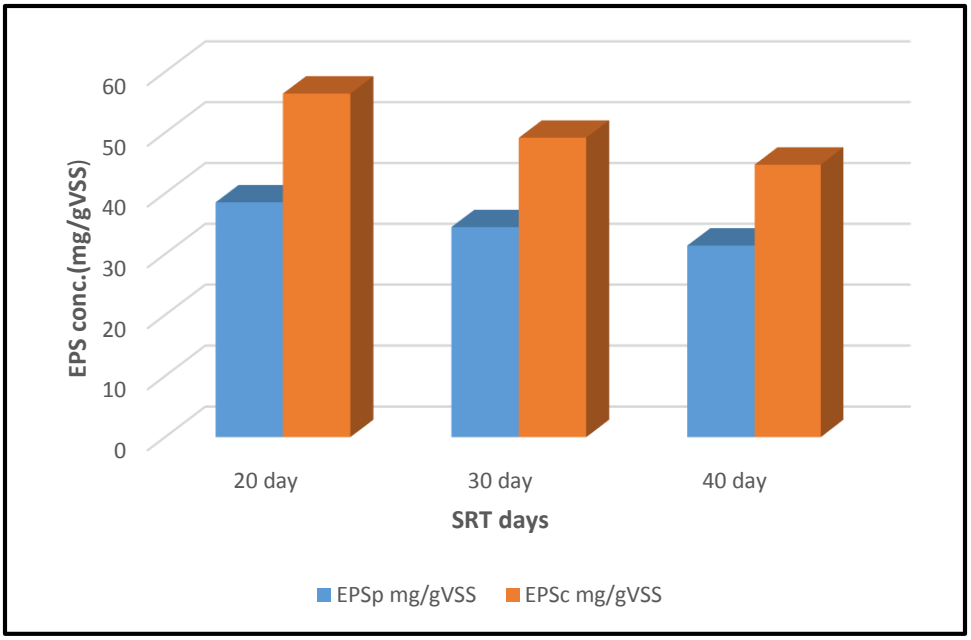


Figure 4. 8 Protein EPS and Carbohydrate EPS of The Reactor Based on Different SRTs

4.1.7 Membrane Plugging and TMP Results

The time course of TMP monitoring for 96 days for each operational SRT phase were shown in figure 4.9. For the 40 day SRT phase, through 19 days, the TMP was exceeding 300 mbar, so 0.2 μm and 0.45 μm membranes were exposed to the physical cleaning. While the pressure grew after 36 days, physical cleaning was no longer effective, thus chemical cleaning was utilized to clean the membrane. For the 30 day SRT phase, physical cleaning was applied to 0.2 μm and 0.45 μm membranes when they were plugged with the sludge after 18 days. A chemical cleaning operation is directly employed for the cleaning of the membranes after 34 days of operation. During the 20 day SRT phase, the TMP was exceeding 300 mbar after 16 operating days, therefore the physical washing was implemented to both membranes and the chemical cleaning was implemented to the membranes after 31 days. New membrane materials were applied to the modules at the end of each phase.

4.1.8 Analysis after Treatment with MBR-NF/Ro

The use of a combination of MBR and NF/RO treatment methods resulted in high rates of removal of most of the chemicals studied in this study. Four contaminants were removed to below limits of detection using a combination of MBR treatment and the NF270 membrane, 79% removal for diclofenac, and about 74% removal for carbamazepine as shown in Table 4.3. MBR and the NF90 membrane provided even higher treatments with the elimination of four pharmaceuticals to below limits of detection, besides 83% and 80% removal efficiency for diclofenac and carbamazepine respectively. When the BW30 was used in conjunction with the MBR treatment, the removal efficiency for diclofenac and carbamazepine were about 86% and 82% respectively, while the concentrations of the other four selected pharmaceuticals in the RO effluent were below the limits of detection.

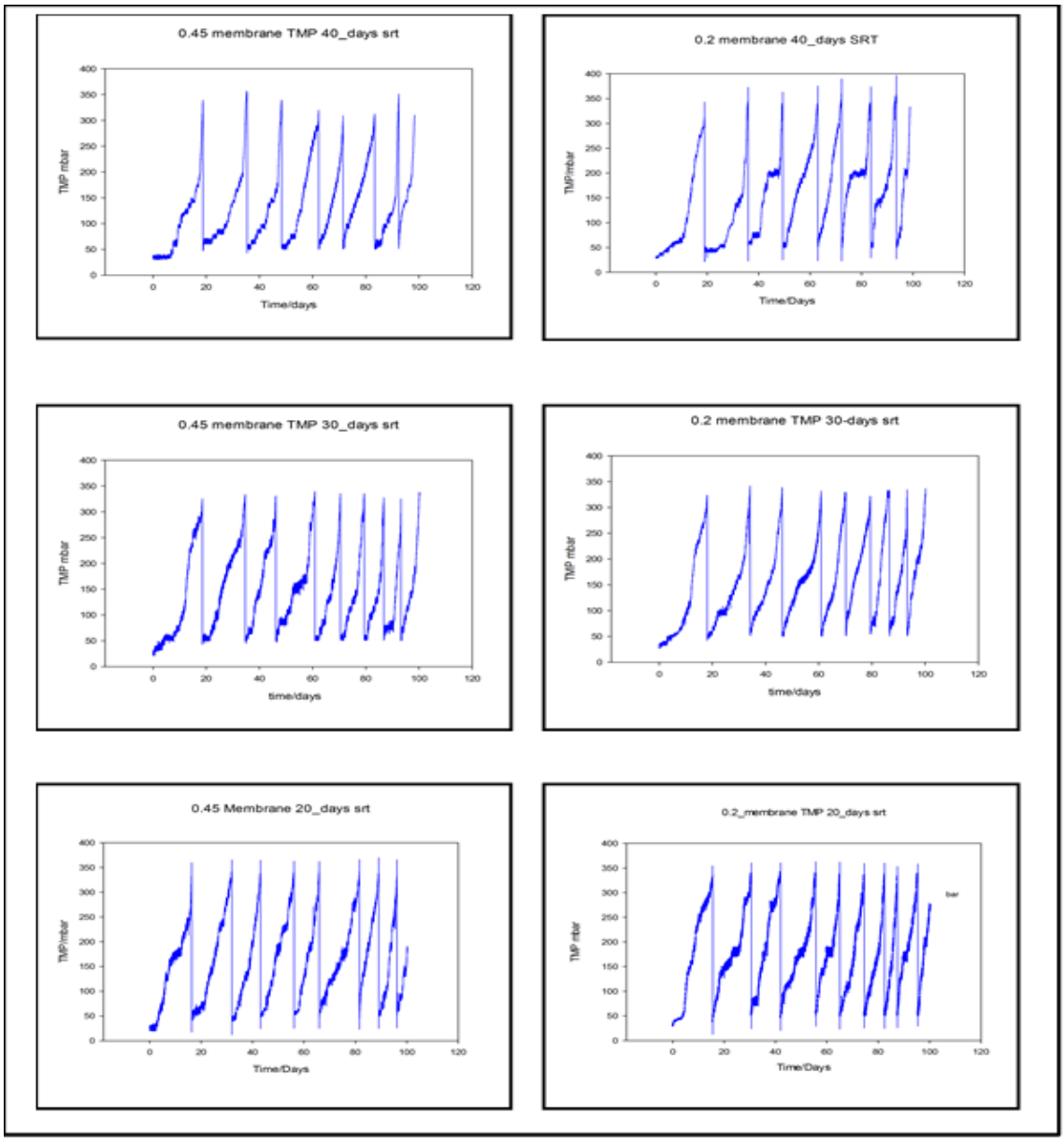


Figure 4.9 Time course of TMP Monitoring for Each 0.2 μm and 0.45 μm Based on Different SRTs

Table 4.3 The Concentrations in (μg/L) of Pharmaceuticals (n=3) before and after Treatments with MBR-NF/Ro

Comp	0.2 μm mem. MBR Eff.	MBR-270 NF Eff.	R.E %	MBR-90 NF Eff.	R.E %	MBR-BW RO Eff.	R.E %	0.45 μm mem. MBR Eff.	MBR-270 NF Eff.	R.E %	MBR-90 NF Eff.	R.E %	MBR-BW RO Eff.	R.E %
DCF	10.173 ± 0.19	2.082 ± 0.024	79.53	1.682 ± 0.031	83.47	1.382± 0.022	86.41	10.49 ± 0.38	2.125± 0.033	79.74	1.739± 0.029	83.42	1.418± 0.031	86.48
BZF	1.72 ± 0.012	< LOD		< LOD		< LOD		1.75 ± 0.024	< LOD		< LOD		< LOD	
CBZ	8.96 ± 0.1	2.263 ± 0.035	74.74	1.806± 0.038	79.84	1.555± 0.027	82.64	9.09 ± 0.08	2.313± 0.036	74.55	1.805± 0.017	80.14	1.551± 0.025	82.93

ATN	2.41 ± 0.043	< LOD		< LOD		< LOD		2.51 ± 0.057	< LOD		< LOD		< LOD	
RND	2.02 ± 0.028	< LOD		< LOD		< LOD		2.028 ± 0.049	< LOD		< LOD		< LOD	
PCT	< LOD	< LOD		< LOD		< LOD		< LOD	< LOD		< LOD		< LOD	

LOD: limit of detection

4.2 Discussion

4.2.1 Discussion of COD Removal, MLSS Concentration, and EMPs Removal in Terms of SRT

At 40 days of SRT, COD removal efficiencies were higher than other SRTs. The MLSS and MLVSS increased by approximately 2 times than 20-day of SRT and 1.5 times than 30-day of SRT. These results are indeed comparable with the study of Broeck et al. (2012) who reported that increasing SRT increases the concentration of suspended solids and a longer SRT would boost COD removal treatment efficiency and produce less excess sludge [143].

Because of high SRT values and complete solid retention inside the MBR, the microorganisms' biodiversity is promoted and even free-living bacteria and slowly growing bacteria remain in the reactor which leads to better performance [144].

The increase in MLSS and MLVSS is widely acknowledged as one of the most significant factors in the biodegradation enhancement of MPs [131].

The MBR treatment shows poor degradation rates of CBZ and DCF and, this may be understood by their characteristics. CBZ is difficult to biodegrade at low concentrations, according to biodegradation research. CBZ did not biodegrade in either sea or freshwater, according to the researchers [145] In addition, The CBZ was classed as “no removal" in some categorization for pharmaceutical biodegradation [72]. CBZ, from the other side, is difficult to adsorb onto the sludge as its (Kd) value is significantly below the value required for considerable absorption onto the sludge [43]. As a result, the bulk of CBZ stays in the aqueous solutions and is filtered by microfiltration membranes. The basis for DCF's low elimination is identical to that of CBZ, except that the DCF's Kd is higher than that of CBZ. Moreover, even though DCF being categorized in the same biodegradability group, DCF is less resistant to biodegradation than CBZ [72]. In comparing the usage of 0.45 μm and 0.2 μm membranes in the MBR treatment, very minor variations were found. This would be consistent with the belief that

the studied pharmaceuticals" principal removal mechanisms during MBR treatment are biodegradation and adsorption into the sludge, rather than being rejected as they pass via the membranes. [146]. The size of target EMPs is in the nm region, and the membranes applied in this study were microfiltration membranes (micron region).

The concentration of all studied compounds was decreased with the increase of SRT. It was observed in Figure 4.2 that MLSS showed an increment in concentration with the increase of SRT. The increase in MLSS should assist the sorption of selected pharmaceuticals [131], [147]. While the increased SRT can generally boost the biological variety of slowly growing bacteria, and longer sludge retention which promotes the MPs removing, some researchers have reported that diclofenac and carbamazepine removal is not affected significantly by SRT changes in MBR treatment [148].

4.2.2 Discussion of SPE Method Adaptation

While ranitidine can be extracted by HLB OASIS, no recoveries were observed by C18 cartridges. For atenolol, HLB OASIS (higher than 86%) gave better recoveries than C18 cartridges (approximately 45%). Similarly, HLB OASIS was more efficient (70%) than C18 for paracetamol. Oasis HLB provided better results for Atenolol, Paracetamol, and Ranitidine comparing to Isolute C18 while Isolute C18 provided better results for Carbamazepine, Bezafibrate, and Diclofenac comparing to Oasis HLB. The recoveries were obtained as 60, 78, and 70% with SPE Method 4, for carbamazepine, bezafibrate, and diclofenac respectively. Accordingly, SPE method 1 was chosen for the analysis of Atenolol, ranitidine, and paracetamol, and SPE method 4 was chosen for the analysis of carbamazepine, bezafibrate, and diclofenac for all the analyses in this study.

4.2.3 Discussion of Removal Mechanisms and Possible Pathways

The pharmaceutical removal mechanisms in MBR treatment are an exceedingly complex approach characterized by four main routes: (i) biotransformation or

degradation; (ii) sorption by the sludge; (iii) volatilization or aeration striping; and, (iv) physical removal through membranes [148]. The constant of Henry's Law for selected pharmaceuticals is lower than $<10^{-6}$, which shows the removal of these compounds by volatilization is negligible (Table 3.1). Moreover, MF membranes usually have molecular weight cut off (MWCO) above several thousand daltons (Da) so that pharmaceutical retention (MWCO from 150 up to 350 Da) is insignificant in the MBR processes because of the exclusion of size. Consequently, biotransformation and sorption by sludge were presumably the dominating removing mechanisms.

For non-ionizable compounds, the hydrophobicity is described as log Kow while it is described as log D for ionizable compounds, a compound is considered as hydrophobic when log D>3.2 or log Kow>2 [134]. pKa values of bezafibrate and diclofenac are 3.61 and 4.15, respectively (Table 3.1) so, they are ionizable compounds, whereas the other pharmaceuticals showed no ionization. Accordingly, all the pharmaceuticals used in this study can be considered hydrophilic except for carbamazepine, which is a moderate hydrophobic compound.

The increased removal efficiency of hydrophobic pharmaceuticals can be due to (i) the dominant sorption by the sludge, which results in enhanced biological degradation, and (ii) having only electron-donating groups (EDGs) that improve oxidation [148]. The removal of carbamazepine is low in MBR processes because of the lack of an electron-donating group. Many other studies have shown that carbamazepine is not removed and recalcitrated in treatment with MBR due to poor degradability [19], [149]. On the other hand, diclofenac was reduced at relatively low efficiency with median removal efficiencies of 49.4%, 42.4%, and 42.1% at SRTs of 40 days, 30 days, and 20 days, respectively. Other researchers have documented a slow or non-biotransformation rate of diclofenac [134], [147]. The lower elimination rate of diclofenac and carbamazepine is due to the existence of multi-aromatic rings in their structure [40]. Paracetamol is highly degraded

because its structure enables bacteria and enzymes to have unobstructed access to the exposed molecule that is later amended [150]. The removal of hydrophilic MPs ranged from 'low removal' (diclofenac) to almost complete removal (paracetamol). The removal of hydrophilic MPs is very clear varying because they have different molecular structures and functional groups. Various removal efficiencies reported for hydrophilic MPs can be express as (i) compounds having only EDGs could accomplish a high degree of removal; (ii) compounds with EDGs and e-withdrawing (EWGs) like amide and chloride in their molecular structure including paracetamol, diclofenac, and atenolol with diverse removal efficiencies; (iii) compounds which are only having strong EWGs like carbamazepine showed low removal efficiency [148]. Therefore, the intrinsic biodegradability of these compounds has a great impact on the dominant removal mechanism of them, as the sludge sorption is less important.

4.2.4 Discussion of Bacterial Community Analysis

In general, the key mechanism for the removal of pharmaceuticals by activated sludge is biodegradation. However, the elimination of environmental contaminants due to the lack of degraders in the environment and the absence of them is not always successful. Biological acclimation and bioaugmentation will overcome all these limitations [151]. Pure cultures and mixed cultures, which can remove the pollutants, can be dominated by biological acclimation and bioaugmentation in the biological treatment process. Pure cultures, which can be used to remove commonly detected carbamazepine, isolating themselves from the activated sludge, wastewater, or sediment. Pure carbamazepine has a stable structure leading to low biodegradability, however, two pure cultures will degrade carbamazepine in presence of glucose, unidentified Basidiomycete [152], and Streptomyces MIUG [152], [153]. White rot fungus Phanerochaete Sordida YK-624 can remove diclofenac entirely and, in the absence of extra substrate can eliminate its lethal toxicity to organisms [151], [153].

4.2.5 Discussion of SMP and EPS Results

During the study, it was observed that SMP and EPS levels were increasing when the SRTs decreased. It has also been observed that as the proportion of SMP and EPS inside the reactor grows, so does the rate of fouling., these results were matched with a study done in the literature [154]. Another study found that increasing polysaccharide levels increased the rate of membrane blockage [155]. According to another study, the increase in EPS was caused by the membrane's resistance increasing [156]. The results acquired from the operating reactor, when viewed in the context of all available data, appear to be comparable to those found in the literature.

Various investigations have shown that the supernatant of activated sludge, which contains colloids and solutes, is more relevant than biological flocs in MBR membrane fouling [157]. As a result, SMP, the main organic element of sludge supernatants, has been identified as important foulants in MBRs [158], [159]. SMPs are soluble (EPS), which are mostly made up of protein, polysaccharides, and humic compounds [160]. Humic SMP, in particular, is thought to be irrelevant to MBR fouling because of its smaller molecular size in comparison to protein and polysaccharides. SMP can also be grouped into two types: UAPs (utilization-associated products) that are formed by substrate metabolism, while BAPs (biomass-associated products) are released due to biomass decomposition. Nevertheless, easily associating MBR fouling with supernatant proteins or polysaccharides concentration or even retention in MBR may not demonstrate the ability to contribute of each element in MBR fouling, because some SMP parts can be managed to retain by the cake layer and not bound to the membrane surface or in membrane pores [161]. As a result, the molecular weight (MW) distribution of SMP has an impact on MBR fouling [162], [163]. Furthermore, physicochemical characteristics of SMP constituents, such as relative

hydrophobicity, may have a major impact on MBR fouling. Proteins, for example, have been found to predominate in foulants desorbed from fouled MBR membrane because of their hydrophobic properties [164]. Operational parameters like organic loadings rates have been mentioned in the literature as issues impacting SMP generation in MBR supernatant [165], [154], [166], [167], SRT and hydraulic conditions like aeration and mechanical mixing [168], [169], and the existence of environmental stress in the wastewater like salts [170], and industrial chemicals such as pharmaceuticals [171], because of the defending reaction or decomposition (lysis) of bacteria as exposing to chemical stress [172]. High SRTs can lessen EPS and SMP concentrations in the mixed liquor by trying to promote starvation circumstances in the MBR, producing a conducive condition for the decreased generation of EPS. Overly high SRTs (50, 70, and 100 days) have been found to increase microbial lysis that produces EPS or SMP that can make a significant contribution to fouling [173]. EPS have been shown to obstruct effluent passage through membranes, by the production of bacteria aggregates in biofilms and flocs, the construction of barriers surrounding the bacteria, the water retention, and the embedment of bacteria in wet gel medium [28]. SMP, in addition can obstruct filtration by blocking pores and forming a gel structure on the membrane surface [174]. As a result, while earlier MBR systems used greater numbers of mixed liquid suspended solids (MLSS) and SRTs (e.g. up to 30 g/L, 100 days), newer MBR systems use reduced and more regulated amounts (e.g. up to 16 g/L, 14 days) to reduce fouling tendency and cleaning frequency [28].

4.2.6 Discussion of Membrane Fouling and TMP Results

Membrane fouling, particularly biofouling, is the most significant impediment to the widespread adoption of MBR technology. Biofouling is the unwanted deposition of microorganisms at a phase transition interface, which can develop as a result of bacterium cells or flocs formation, growth, and metabolism on the membranes [175]. Biofouling is among the most critical operational difficulties in membrane processes, since it limits flux, diminishes membrane efficiency, and

raises membrane replacement, as well as operational and maintenance expenses. At the 20 day SRT phase of this study, the fouling occurred much more often and faster for both 0.2 μm and 0.45 μm membranes than the fouling occurred during the 30 and 40 day SRT phases. One of the reasons might be the increase in the values of SMP and EPS when decreasing the SRT. The low MLSS concentrations are another cause. Various types of results have been found in the literature to criticize the effects of MLSS concentration on membrane filtration performance [176]. Low MLSS concentrations (< 6 g / L MLSS) have also been shown to produce blockage [28]. For this reason and to observe stable state operation in MBR, MLSS concentration should be at least 6 g / L.

Total resistance R_T in the MBR is the summation result of the intrinsic membrane resistance R_M, the cake resistance R_C, and the pore blocking resistance R_P.

SMP (including SMP_C and SMP_P) on the membrane surface induced higher cake layer resistance R_C in the MBR. Because of the strong drag force supplied by the permeate pump, more SMP_C and SMP_P might be adsorbed and/or bound to the membrane surface at high TMP. Smaller sludge flocs may cause serious membrane fouling due to pore blockage and cake formation, and induced higher TMP increment rate. Higher R_C and R_P in the MBR were attributed to the existence of smaller sludge flocs. Due to greater shear produced dispersion and inertial lift force, bigger particles could not simply deposit on the membrane surface. In addition, as mentioned before, the presence of SMP in activated sludge seems to play a significant role in first membrane fouling. Membrane fouling progression, on the other hand, was mostly influenced by bound EPS in activated sludge at a later stage. Caused by the combined effects of pore clogging and adsorption on membrane walls and within membrane pores, SMP has been believed to improve fouling propensity. [177]. As a result, higher SMP concentration in the MBR cake layer resulted in higher R_P, which was in line with Jamal Khan et al finding's (2012) [178]. Besides, in the MBR, a larger content of bound EPS in activated sludge may enhance both R_C and R_P. A dense fouling layer of microbial cells coated

with EPS was detected on the membrane, which closed membrane pores [179]. In addition, Meng et al. (2006b) discovered a substantial positive association between the total amount of EPS and the fouling resistance induced by pore plugging and cake formation [180].

Membrane fouling in the MBR was caused by both SMP and EPS (particularly SMP_C and EPS_C). Polysaccharides, unlike proteins, have a partly hydrophilic character that allows them to enter the cake layer and membrane pores, as well as cause permanent fouling. [181], [175].

4.2.7 Discussion of MBR-NF/Ro Analyses

The results in Table 4.1 demonstrate that MBRs are limited in their ability to remove several hydrophilic and biologically stable trace organic chemicals. However, because the majority of these harmful chemicals are hydrophilic, NF/RO membranes could be used to more effectively eliminate them. In addition, as shown in Table 4.3, NF/RO membranes can be an excellent complement to MBR treatment, removing almost 99% of the trace organic pollutants used in this investigation. According to Nghiem et al. [182], some hydrophobic substances may be removed at a lower rate than expected. This is due to the ability of hydrophobic chemicals to attach to NF/RO membranes and subsequently diffuse through the thick polymeric matrix, resulting in significant transport of these chemicals throughout the ultra-thin active skin layer. Hydrophilic trace organic pollutants, on the other hand, can be successfully rejected by NF/RO membranes via steric hindrance or size exclusion mechanisms since they do not absorb to the membrane polymeric matrix. The NF270 is a high-permeability loose NF membrane with large open pore size. As a result, the NF270 membrane's removal efficiencies for diclofenac and carbamazepine were lower than those of the NF90 and BW30 membranes. This holds true for both the tight NF membrane NF90 and the RO membrane BW30 studied in this work. Because the vast majority of the chemicals chosen are hydrophilic ($\log D < 3$), no appreciable adsorption of these hydrophilic molecules to the membrane is expected. The findings support the

ability of low-pressure RO and, to a lesser extent, NF membranes to operate as effective barriers against hydrophilic and large-molecular-size trace organic molecules. These findings further demonstrate the value of combining NF/RO membrane filtration with MBR treatment to remove hydrophobic trace organic molecules in a complementary manner.

4.3 Conclusions

The biodegradation of six pharmaceuticals was investigated by membrane bioreactors. After the reactor reached steady state conditions, the degradation efficiencies of six targeted pharmaceuticals were determined under different sludge retention times. The highest degradation efficiencies were observed for paracetamol for each SRT and followed by Ranitidine, Atenolol, Bezafibrate, Diclofenac, Carbamazepine. The bacterial community analysis was evaluated for the sludge on steady-state conditions and also after adding the pharmaceuticals. It was observed that Proteobacteria in the sludges increased from 46.8% to 60% while Actinobacteria increased from 9.1% to 17.9%. This reveals that microorganisms can metabolize the targeted pharmaceuticals. To understand the degradation mechanism, possible by-products were observed in the effluent samples, where the first step degradation by-products of diclofenac, bezafibrate, and carbamazepine were detected. As a further study, the ratio of sludge adsorption and degradation of targeted pharmaceuticals can be studied to understand well whether the sludge requires additional treatment. Since the degradation of diclofenac and carbamazepine is still needed to be degraded, the development of highly effective biodegradation of these compounds should also be focused on.

The findings of this study show that NF/RO membrane filtration and MBR treatment can work well together to improve the removal efficiency of trace organic pollutants. MBR is capable of removing hydrophobic and biodegradable trace organic molecules efficiently. Because of their quick adsorption to the MLSS, these hydrophobic chemicals have a longer residence time in the biological

reactor. Hydrophilic trace organic molecules, on the other hand, were successfully eliminated by the three NF/RO membranes used in this investigation. It's worth noting that the BW30 RO membranes are low-pressure RO membranes. It has long been thought to be appropriate for nonpotable and indirect potable water reuse. The coupling of MBR and the low-pressure RO membrane BW30 resulted in bezafibrate, atenolol, paracetamol, and ranitidine being removed to levels below the quantitative limits of detection. It has also the highest removal rates for diclofenac and carbamazepine. Despite RO is an effective removal method, it cannot be used as an absolute barrier to some OMPs because some pharmaceuticals were found in the permeate over their LOD. Therefore, additional treatment techniques, like adsorption to activated carbon or advanced oxidation processes may be achieved to be incorporated with the RO to ensure complete removal of such pharmaceuticals.

Membrane fouling in the MBR was controlled by SMP and bound EPS of activated sludge in the early stages and later stages. With a lowering in SRT, the steady-state fouling rate of both 0.2 and 0.45 m membranes increased linearly. The optimum operating SRT for MBR in this study was 40 days. Longer SRTs are preferred for better biomass retention, which leads to better treatment efficiency and the domination of slow-growing microbes capable of consuming macromolecules like polysaccharides, carbohydrates, and proteins. Extremely long SRTs, on the other hand, might result in the accumulating of dead and inactive bacteria, reducing sludge action.

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PUBLICATIONS FROM THE THESIS

Papers

1. Alobaidi, R.A.K., Ulucan-Altuntas, K., Mhemid, R.K.S., Manav-Demir, N. and Cinar, O., 2021. “Biodegradation of Emerging Pharmaceuticals from Domestic Wastewater by Membrane Bioreactor: The Effect of Solid Retention Time” International Journal of Environmental Research and Public Health, 18(7), p.3395. https://doi.org/10.3390/ijerph18073395

Projects

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