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THE REMOVAL OF PHARMACEUTICAL COMPOUNDS FROM WATER USING MEMBRANE PROCESSES: PERFORMANCE, MECHANISMS, AND THE EFFECT OF SALT.

by
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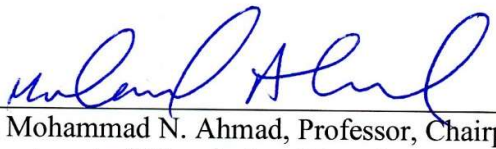

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AN ABSTRACT OF THE THESIS OF

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Title: The Removal of Pharmaceutical Compounds from Water Using Membrane Processes: Performance, Mechanisms, and the Effect of Salt

The occurrence of several categories of pharmaceutically active compounds (PhACs) has been reported in different water bodies all around the world. The risks of this issue are still not fully understood, however, the exposure to a plethora of PhACs creates a matrix effect that is bound to have repercussions on the environment and may constitute a "human health risk". The properties of these contaminants and the bodies in which they exist are diverse, so their removal proves to be a challenge for conventional water and wastewater treatment technologies. Membrane processes, such as nanofiltration (NF) and reverse osmosis (RO), have gained popularity over recent years as an effective treatment technique for the removal of contaminants of emerging concern from water.

This study aimed at evaluating the performance of a bench-scale membrane unit in removing PhACs from various water matrices. It investigated the removal of three common pharmaceuticals, individually and as a mixture: carbamazepine (CBZ), ibuprofen (IBF), and diclofenac (DCF). In addition, the influences of the PhACs properties, membrane types (NF, RO) and salt concentration on the removal process were studied.

The effects of salt and the PhAC mixture were found to be more pronounced for NF membranes rather than RO, and for compounds with smaller molecular weights. These effects, when present, also varied based on the properties of the compounds such as the charge, size, and hydrophobicity, thus enhancing retention in some cases while reducing it in others. High rejection values (>99%) were reported for all PhACs in RO filtration at all salt concentrations. However, NF retention values varied for the different PhACs based on their properties as well as on the salt concentration. DCF rejection with NF was found to be high (90-99%) as well as IBF rejection (85-96%) and increased with increasing salt concentration. Moderate retention values were found for CBZ (65-77%) and decreased with increasing salt concentration. All salt effects were buffered by the introduction of the PhAC mixture.

Keywords: Nanofiltration, reverse osmosis, membranes, pharmaceuticals, salt

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CHAPTER 1

INTRODUCTION

The increase in the demand for fresh water is a worldwide issue, and a large portion of the available fresh water bodies are under constant contamination. Wastewater effluents are a major source of micropollutants in the water cycle, and these pollutants eventually find their way on to drinking-water supplies like rivers, lakes, or groundwater aquifers.[1] Several environmental contaminants, including but not limited to endocrine disrupting compounds (EDCs), and specifically pharmaceutically active compounds (PhACs), have been detected globally and are a cause for concern due to their adverse effects on the environment and on public health.[2] Long term exposure to pharmaceuticals, even at trace levels, have been proven to have caused hormonal disruptions in fish and the decline of bird populations in some parts of the world.[3,4] This is besides the potential risk that the increase and compilation of pharmaceuticals in the environment could pose to humans in future.

Conventional wastewater systems can partially remove some pharmaceuticals, however most compounds are not removed and are consequently detected in the outlet streams.[5] These systems generally use activated sludge to treat wastewater according to environmental standards, however concentrations of pharmaceuticals in the effluent are currently not regulated. In addition, many pharmaceuticals have hydrophilic characters, which limits their sorption to sludge, and water-soluble compounds in the sludge could potentially leach to groundwater or run off to surface water which further adds to the

problem.[6,7] This gives rise to an interest in studying and refining wastewater and drinking-water treatment technology in order to better understand these processes.

To effectively remove pharmaceuticals from sewage and drinking-water, advanced treatment techniques should be used to replace or add to conventional systems.[2] Advanced treatment could be a chemical process which includes advanced oxidation, such as ozonation, and has the capacity to degrade pharmaceuticals, however these techniques are usually expensive and complicated and may result in hazardous degradation byproducts.[8] Some physical processes, for instance adsorption by activated carbon or membrane processes, can also efficiently remove pharmaceuticals and these techniques are generally more widespread.[9] The removal of pharmaceuticals by activated carbon may be influenced by many factors including chemical structure, solubility, and competition for sites on the carbon, resulting in the persistence of some molecules like diclofenac or ibuprofen.[9,10,6]

Membrane separation is a physical process that has gained a lot of popularity and has shown good overall rejection values for pharmaceuticals.[11] Both reverse osmosis (RO) and nanofiltration (NF) are pressure driven separation processes with similar modes of action that can produce a permeate free from a wide range of contaminants including pharmaceuticals.[12] In general the retention of pharmaceuticals by NF and RO is influenced by several factors such as the membrane properties (pore size, charge, fouling), water quality (pH, ionic strength, temperature, natural organic matter (NOM)), and physiochemical properties of the pharmaceuticals (molecular weight, size, charge, hydrophobicity).[13] The mechanisms by which pharmaceuticals are rejected from or transported through the membranes are discussed later in this work,

and most of this information is derived from studies of bench-scale membrane units that are used to test specific aspects of the process in order to gain a better understanding.

For example, Nghiem et al. used NF membranes to investigate the removal of hormonal steroids. This heavily cited work considered three main removal mechanisms and employed a mathematical model to predict the membrane pore size.[14] Another study using the same NF membrane (NF270) and an RO membrane (XLE), was conducted by Lin et al. and attempted to elucidate the rejection mechanisms of multiple pharmaceuticals and identify the role of adsorption in retention. In other cases, a large number of pharmaceuticals were used in order to glean certain patterns; 52 EDCs and pharmaceuticals were studied by Yoon et al. in nanofiltration and noted that hydrophobicity is a very important factor, and this was confirmed by other studies.[15-17]

Other bench-scale studies aimed to test the efficiency of certain membranes in real or simulated water matrices in order to test the feasibility of a full scale unit, which was found to be not economically feasible in some cases,[18] whereas in other cases it was found to be a cost-effective technique.[19] In fact membranes are already being monitored for their efficiency in pharmaceutical removal in full-scale plants. Al-Rifai measured the concentrations of 13 micropollutants in a full-scale RO wastewater plant for over a year, and he found that the rejections were high with the exception of Bisphenol A.[20] Membrane separation is also used for drinking-water treatment, as Radjenovic et al. monitored the removal of pharmaceuticals in ground-water and their rejections after their treatment with NF/RO and found that it correlated with the molecular size of the compounds even at trace-level concentrations; moreover, concerns were raised on the disposal of the concentrated brine reject of the process.[21] This gives rise to an interest

for the prediction of the process outcomes since full-scale applications require large financial investments, however the process is hard to model due to the many factors influencing the performance.[22] Nevertheless, there have been some attempts at constructing a full-scale mathematical model to predict the rejection of pharmaceuticals and other contaminants, besides the attempts to model bench-scale processes to study the mechanisms, as will be discussed later.[23]

Regardless of the difficulty in analyzing the multiple factors affecting the removal process, the further study of these influences remains an objective in research. The ionic strength, which is usually represented by the amount of salts in the feed and has an important role in industrial applications, is selected to be considered in this study.[24] For example, food processing, pharmaceutical synthesis, and other biochemical industries often produce waste streams concentrated with salt (NaCl) up to 20% by weight.[25] A comprehensive review of different salt effects on membrane filtration was reported by Luo et al. and provided a good summary of some of the work done on the effect of salts on membrane properties and performance.[24] Regarding the filtration of pharmaceuticals specifically, the ionic strength effects have been discussed in different works. Nghiem et al. considered the influence of ionic strength when studying the role of electrostatic interactions, and found that monovalent salts could affect the Debye length of pharmaceutical molecules and that they behave differently than divalent salts.[26] Ren et al. recently reported on an increase in retention values of ibuprofen while using nanofiltration, when NaCl was added compared to no salt in the feed.[27] An overview of the mechanisms behind the effects that salts can have on membrane filtration is also discussed in the next section, along with the mechanisms of removal.

RO and NF membranes have become a commercially accepted desalination techniques in the last couple of decades, making the study of the effect of salts on other contaminants during the filtration process a point of interest, especially monovalent salts that tend to remain even after pretreatment.[28] The disposal of the concentrate produced by the process is a challenge especially in inland areas, hence concentrating the reject to small manageable amounts, using membrane processes, is preferred.[29,30] The effect of high salt and contaminant concentrations, pharmaceuticals in this case, on membrane filtration is thus important to consider.

This thesis aims to study the removal of three different pharmaceuticals by two commercially used membranes, DOW Filmtec's NF270 and XLE membranes in a concentration mode of filtration. Moreover, the effects of the monovalent salt sodium chloride (NaCl), at different concentrations, on the removal of these pharmaceuticals is studied, along with speculations on the mechanisms responsible for these effects. In addition, one objective was to consider any possible effects that the mixture of pharmaceuticals may have on the membrane filtration process, as a mixture is usually the case found in full-scale treatment. To the author's knowledge, the pharmaceutical combination effect on NF and RO has not yet been reported in the literature. The pharmaceuticals in this study are commonly used worldwide, and were shown to be priority contaminants in Lebanon.[31] The pharmaceuticals used with the experiments will be spiked at a concentration of 10 mg/L; this value is relatively high compared to the concentrations found in surface and ground waters, however this is selected in order to enable easier analytical procedures due to the detection limits of the instrument. Furthermore, the effect of increasing pharmaceutical concentration on NF/RO membrane performance has been studied and no significant effect was reported, hence

increasing these concentration in the experiments is not expected to have an effect on retention.[32] The study is to be conducted on a bench-scale batch membrane system, and the results will then be used to consider the mechanisms that could be involved in the rejection of these pharmaceuticals.

CHAPTER 2

TRANSPORT THEORIES

The following chapter will discuss some of the theories related to the transport of molecules through membranes, and the mechanisms by which they are retained. A literature review will be conducted on the possible effects that salts have on the removal process on a molecular level. Moreover, a mathematical predictive model will be suggested and discussed in relevance to the present study.

2.1 Rejection Mechanisms

The transport of solutes through NF membranes has been studied extensively in the literature. Since nanofiltration lies between ultrafiltration and reverse osmosis, in terms of pressure and porosity, the mass transfer is usually a combination of convection and diffusion.[33] When it comes to rejecting trace organic compounds such as pharmaceuticals, the separation process is accomplished generally through three main mechanisms: size exclusion, electrostatic repulsion, and adsorption. These are chemical and physical separations that are affected by the physicochemical properties of the membrane, the solutes, and solution chemistry.[34]

Although many authors have tried to model the transport of electrolytes and solutes through NF membranes over the past few years, it has proven difficult to predict the outcome of the performance of these processes i.e. the rejection, flux, fouling capacity.[22] The end goal is to predict the separation selectivity between the various ions

and components in different solution matrices, so that the process can be fully optimized for different conditions of operation.

Some of these approaches include the Maxwell-Stefan equations which describe the diffusive movement of species in a stationary state. In these equations the driving forces working on a species are equal to the friction of that species with other components in the system. However, knowledge of all the species friction coefficients in a system is difficult, especially that it is affected by the solution environment like the ionic strength.[22] Other models include the modified solution-diffusion model which is based on the classic model yet assumes a porous structure, and describes the observed rejection of a solute as a function of water flux and membrane structural factors.[35]

Another approach is the extended Nernst–Planck equation, which describes solute transport as a combination of diffusion, convection, and electro-migration, based on Donnan potential, and assumes a low salt concentration inside the membrane pores.[35] It could be thought of a simplified version of the previous model, however it is used more frequently in the literature due to its simplicity and smaller number of parameters.[36]

Models like these are usually based on the laws and mechanisms linking the parameters to the experimental conditions to predict the rejection for a given feed solution.[36] Even though these predictions, could approach experimental results, it is still not fully understood how the interactions between these mechanisms occurs and it is not fully possible to predict the outcome.[22]

Thus a comprehensive understanding of the rejection mechanisms of various contaminants, in this case pharmaceuticals, and the factors that affect them is crucial for the prediction of the outcome, optimization of the process and development of new applications.[37] PhAC transfer through nanofiltration is of interest since rejection values have been known to vary across the literature. The main mechanisms governing the transfer will be discussed, along with the effects and mechanisms salts may have on the transfer, to gain a better understanding to model the transport of the process.

2.1.1 Size Exclusion

The terms size exclusion, steric hinderance, and sieving effect have been used interchangeably and they all refer to a retention mechanism that is based on the physical size and shape of the molecule or contaminant. Simply put, any solute larger than the pore size of the membrane is excluded into the reject and cannot permeate the membrane.[34] It is important to note that this mechanism is different from the classical sieving, such as in micron filters, since membrane pores and solute species do not have a uniform size.

It is difficult to account for the variety of situations in the various membranes and solution chemistries especially when trying to model the process solely based on this mechanism. However, it is useful to characterize the factors affecting size exclusion in order have a more complete understanding of the process.

The simplified assumption of the mechanism assumes that cylindrical capillaries exist within the membrane structure and the pore size is this capillary diameter, whereas the contaminants and solutes are assumed to have a spherical shape.

The size of these compounds is then assumed to be related to their molecular weights (MW). One way to predict how this mechanism will have an effect is to compare the MW of the compounds to the molecular weight cut off (MWCO) of the membrane, which is usually given by the manufacturer, and corresponds to 90% rejection of solutes with a molecular weight higher than that value.[34]

Even though molecular weight is the most used parameter to reflect molecular size, studies have shown that it is a poor direct measure of the actual size, and does not fully predict rejections when it comes to PhACs.[16] The molecule structural elements such as length, width, depth, and volume all play a role in how solutes interact with the membrane surface. Kiso et al. have shown that molecule width is more correlated to rejection values than MW, meaning that the shape of the molecule is an important factor in steric hindrance.[38]

Molecules' shapes and sizes cannot be represented fully by spheres, as their size and shape are flexible and affected by solution chemistry. For example some large molecules fold out into linear chains when exposed to high pH due to electrostatic repulsions.[34] Nevertheless a good indicator used often is the effective size or Stoke's radius and is calculated by the following formula:

$$r_s = \frac{kT}{6\pi\eta D_s} \qquad (1)$$

where k is the Boltzmann constant (J/mol.K), η is viscosity (kg/m.s), T is temperature (K) and D_s diffusion coefficient (m^2/s). The diffusion coefficient term D_s can be estimated using the Wilke Chang formula[39]:

$$D_S = 1.193 \times 10^{-7} \frac{M_S^{0.5} T}{\eta V_S^{0.6}} \qquad (2)$$

M_s and V_s represent the solute molecular weight and molar volume of the solute respectively.

When considering solute transport through nanopores as convective and diffusive, one will notice that the ratio of the size of the pores and molecule size will have a large effect on the rejection. This is represented by λ, the ratio of effective radii of the solute to the membrane pore radius. In fact, this parameter is present in most models that consider convective flow.

The rejection of micro-pollutants like trace organic compounds (TrOCs) and specifically PhACs has been shown to be dependent on membrane characteristics and types. Usually when the molecular weight of the contaminant is much larger than the membrane molecular weight cut off, high rejections are expected and observed. However, when the molecular weight of these substances is close to the membrane molecular weight cut off, other factors like the surface charge and hydrophobicity start to play larger roles in the retention behavior.[40] For pharmaceuticals, the molecule sizes usually range from 200 to 500 g/mol [41] and this value is close to the MWCO of most nanofiltration membranes meaning it is difficult to predict the rejections based on size exclusion alone but it does play a vital role.

2.1.2 Electrostatic Interactions

Charged solutes in the feed are known to be affected by electrostatic interactions in membrane filtration systems. At neutral pH, polyamide membrane

surfaces are usually negatively charged. The membrane active layer contains ionizable functional groups, like carboxyl and amine groups, that dissociate at neutral to high pH values.[42] The membrane surface charge is usually measured by zeta potential experiments, and the values for many commercial membranes have been reported in the literature.

Contaminants in solution could also have a charge based on the pH of the feed. This is quantified using the acid dissociation constant (K_a) which measures the ability of an acid to donate a proton to a specific reference base (i.e. water in the case of filtration of pharmaceuticals). The pK_a, defined as $\log(K_a)$, can determine the percentage of the dissociated species of the solute and classified as a positively, negatively charged or neutral fraction.

The negative charges on NF membrane surfaces interact with ions and charges in solution and allows the repulsion of negatively charged solutes to enhance the removal rates. This can be described as the Donnan exclusion principle.[43] On the other hand, positively charged solutes may become attracted to the negative membrane surface and cause what is termed the charged concentration polarization.[44] In addition, the membrane charge can also affect neutral solutes through polarity effects. It was demonstrated that the electrostatic interaction directs the dipole moment of molecules towards the membrane and decreases the retention.[45]

Eventually a buildup of concentration between the charged components and the membrane surface is achieved, and this leads to an osmotic pressure difference between the membrane and solution. This pressure difference is compensated for by the Donnan

potential and it is affected by several factors including the salt concentration, ion valences in solution, and charge concentration on the membrane which varies with solution pH.

2.1.3 Adsorption and Solute-Membrane Interactions

Adsorption is the adhesion of molecules or ions on a surface because of the chemical or physical interactions between them. Physical adsorption is due to electrostatic and dispersive interactions and is usually reversible, however chemical adsorption can be irreversible like polymerization or a result of weak reversible chemical bonds such as hydrogen bonding and complexation.[34]

Membrane systems can have both types of adsorption acting. Since both the membrane and the contaminants can be organic materials, hydrogen bonding is a possible mechanism of adsorption. As for the physical type, hydrophobicity properties of both can dictate the extent to which it occurs. Moreover, this membrane mechanism is not only limited to the adsorption of compounds, but also the polar interactions that occur on the membrane surface and within the membrane pores.[46]

A good measure of hydrophobicity in the contaminants is the octanol-water partition coefficient or log K_{ow}, which is the ratio of the concentration of unionized compounds in the octanol phase to the concentration in the water phase at equilibrium, or sometimes used as log P and takes into account charged compounds. With organics and pharmaceuticals, a log K_{ow} value greater than 2 is said to be hydrophobic, and as such, can be adsorbed on the membrane surface.[47]

Diffusion plays an important role in most transport models, and adsorption may have a strong influence on diffusion. In a study by Ngheim et al. it was demonstrated that lower rejection values for hormonal compounds were found vs the predicted rejections by a model based on solute transport through a nanoporous membrane. The reason being the likely adsorption of the compound on the membrane pores and subsequent diffusion into the permeate, resulting in lower retention rates.[14]

On the other hand, the adsorption of compounds on the membranes could support the retention of contaminants, as Kiso et al. found that retention for pesticides increased with increasing hydrophobicity and that it had a strong correlation with the octanol-water partition values of the molecules.[17] This correlation is in contrast to the one found by Van Der Bruggen, where for molecules with comparable molecular sizes to the MWCO of the membrane, the octanol-water partition coefficient was inversely related to the rejection values. He also found that the influence of hydrophobicity on rejection values decreases as the molecular size, compared to the MWCO, increases.[48]

The influence of adsorption was tested in other studies, for example systems operate in full circulation mode were observed, and neutral hydrophobic pharmaceuticals were shown to adsorb on the membrane and subsequently diffuse into the permeate.[41] It was also shown that even having the membrane in contact with some pharmaceuticals in a flask resulted in the adsorption of a small amount on the surface and in the pores.[41,49]

2.2 Salt Effects on the Mechanisms:

This research focuses on the rejection performance of pharmaceuticals from NF/RO membranes and in addition the effect that the inorganic monovalent salt sodium chloride (NaCl) has on the rejection mechanisms. The influence of salts can be classified as two effects, with one affecting membrane properties and the other affecting the neutral and charged solutes.[27] In general, the addition of salt into the water matrix would decrease retention values, however in some cases the opposite is true. The influence of salts, like the rejection mechanisms, depends on the nature of the membrane, the salt, and the solute being studied.[24] A survey of some of the reported effects that salts have had on membrane filtration processes, and the presumed mechanisms behind the effects is presented.

2.2.1 Membrane Properties

a. Pore Swelling:

One of the ways by which salts affect membrane properties is through modifying the pore radius by pore swelling. This swelling effect is well accepted, however there has not been a physical observation of the phenomenon.[24]

In a study considering the effect of salts on the retention of glucose, it was found that the addition of salt ions resulted in a reduction of glucose retention. It was

hypothesized that the reason behind this decrease is a high surface charge in the membrane pores as a result of the high concentration of salts in the pores, and this effect was predicted by the model used in the study. These charges may cause high repulsion forces, thus swelling the pores of the membrane meaning a larger pore radius, which would then translate into lower retention values by size exclusion. This effect is dependent on the salt ion and the membrane itself. Interestingly, a positive correlation was found between salt retention and the glucose retention, as the salts that had a lower retention, like NaCl, had a larger effect on the glucose retention.[50]

The pore swelling effect was also found in another study by Escoda et. al. where the rejection of polyethyleneglycol by nanofiltration was investigated. Salt addition was found to decrease the rejection values, and the higher the salt concentration the larger the drop in rejection. Moreover, their work was compared to their previous study with the use of ceramic "rigid" membranes and it was found that pore swelling indeed did have an additional effect on the polymeric membranes. Again, salt ion adsorption was attributed to be the mechanism behind the pore swelling, as the membrane charge density increases with salt concentration, resulting in the compensation by the migration of the salt counter-ions inside the pores. This leads to pore swelling because of the electrostatic repulsions between the counter-ions.[51]

Although there have been no reports of a direct observation of the pore size changing, it has been concluded from modeling results that this is the case. Atomic force microscopy is not accurate enough to distinguish variations in membrane pore size.[24] Luo et. al. found that based on the extended Nernst-Planck equations, it was concluded the solute-to-pore size (λ) ratio decreased with increasing salt concentrations.

He proposed that the hydrated layer in the membrane pores could become thinner due to the salt effects and result in an increase in pore size.[25]

b. Membrane Charge

Alteration of the pore size is not the only way by which a membrane is affected by salts, since as mentioned before, membrane surfaces are usually charged due to the ionization of functional groups on its surface; salt ions in solution naturally influence this charge. The Donnan potential is highly influenced by the valence of the ion present and the concentration of the salts in solution.[43]

An electrostatic interaction exists between the surface and the ions because of the presence of negative and positive charges on the surface of the membrane. Screening of the overall membrane charge may occur as a result of this interaction, which is an adsorption of ions on the surface referred to as counter-ion site-binding. Moreover, the hydrophobic nature of the surface also induces a competitive adsorption of ions due to non-electrostatic forces. These mechanisms along with the dissociation of the functional groups all play a role in the membrane surface charge, which in turn plays a role in the rejection of charged contaminants.[52]

Charge behavior versus salt concentration depends on the salt type and mainly its size and valence. For NaCl specifically, in a study by Bruni et. al., it was found that for a salt concentration greater than 300 ppm, the site-binding effects of sodium and chloride are so strong that the membrane charge due to the acid/base dissociation is completely screened by the bound ions. In addition, at a constant pH value, as the salt

concentration increased the membrane surface charge also increased.[52] In another study measuring the zeta potential of nanofiltration membranes, as salt concentrations increased the magnitude of zeta potential decreased.[53]

2.2.2 Salt effects on the solute properties:

In addition to the effects inorganic salts have on membrane properties, some solute properties have been reported to vary in the presence of concentrated salt solutions. Neutral organic compounds are affected by a phenomenon called the "salting-out" or "Hofmeister" effect. This means that water molecules would preferably solvate ions thus causing a partial dehydration to the neutral molecules. These molecules would then have a decreased effective size resulting in easier transfer through the membrane pores and lower retention rates in membrane processes based on the steric hindrance model.

The study with ceramic membranes that was mentioned previously, considered the influence of salts on the rejection of polyethylene glycol. Since the membrane materials do not allow for swelling, and a decrease in rejection was observed, the salting-out effect was proven to be significant in the retention, and was also quantified using modeling techniques.[54] In another series of experiments, Boy et al. developed a procedure to dissociate the influence of salts on the solute properties from those on the membrane properties. Indeed the dehydration of polysaccharides was observed, and that the transfer of these molecules depended on the nature and the concentration of the salts present in solution.[55]

Ngheim found that even charged organic molecules could be dependent on solution ionic strength. He argued that the Debye length is an extension of the functional groups and it decreases with increasing salt concentrations. Hence, a variation in ionic strength could be a determining factor for the rejection of charged molecules by charged membranes.[26] In a recent study showing the effects of salts on ibuprofen retention, a complexation mechanism was suggested. It considered the complexing of calcium ions in solution and on the membrane surface with the functional group of ibuprofen, thus blocking the molecule from entering the membrane free volume.[27]

The salting out effect is also present when discussing the solubility of organic compounds in water. It has been demonstrated that the higher the salt concentration in an aqueous solution, the less soluble most organic compounds are.[56] In addition, the co-ion effect might influence the solubility, for example the addition of sodium chloride could reduce the solubility of Ibuprofen-Sodium. Low solubility could be an indicator for better rejections in membrane filtration processes.[16]

Finally, salt concentrations could influence the polarizability of compounds causing a change in the dipole moment of the molecule and consequently its interaction with the membrane.[57] Log K_{ow} values also increase with increasing salt concentration, and this means the compounds become more hydrophobic leading to easier adsorption on the membrane or an induced charge effect.[58] Hence, careful consideration of the effect of salts is necessary before assuming the effect it will have on the final process.

2.3 Modeling

Attempting to mathematically model the filtration process is useful to check which described mass transfer mechanisms are dominantly in action. Moreover, successful models can also help in optimizing the process and its operational conditions, and in selecting the most suitable membrane for the contaminants.[59] Models have been developed in the literature describing rejection in both NF and RO membranes.[23] Regarding RO however, to this day there is no general consensus on the porosity of the membrane or the transport of materials through the membrane, and no conclusively accepted model to describe the transport.[60] For the sake of this work, the XLE RO membrane will be treated as a tight NF membrane; both are presumed to be porous and the same transport model is assumed.

A commonly used transport model is the Donnan steric pore model and dielectric exclusion (DSPM-DE) model, and it is derived from the extended Nernst–Planck equation and considers a Hagen–Poiseuille flow pattern through the pores.[61] However, this model was not able to correctly predict the rejection of organic matter, especially pharmaceuticals, since more than one mechanism is assumed to be involved in retention, resulting in an over-prediction when applied.[59,62] For the sake of practicality, the hydrodynamic model will be used to describe the transport, and it assumes the membranes have cylindrical pores with a uniform radius, and that the transport is due to convection and diffusion.[14]

$$J_s = -K^{-1}D_\infty \frac{\partial c}{\partial z} + GVc \qquad (3)$$

J_s is the solute flux, V is the fluid velocity, c is the solute concentration, D_∞ is the Stokes-Einstein diffusion coefficient, z is the axial position along the cylindrical pore, K is the enhanced drag, and G is the lag factor. The hydrodynamic coefficients K and G account for the finite pore sizes and depend on λ, the ratio of solute radius (r_s) to the pore radius (r_p) . The solute radius is estimated using the Stokes-Einstein and Wilke-Chang formulas (equations 1 & 2) mentioned earlier. The pore radius was calculated in the literature by using tracer compounds and fitting models to calculate the radius.[37] The λ is used to estimate a distribution coefficient $\Phi = (1-r_s/r_p)^2 = (1-\lambda)^2$. This coefficient is equal to the equilibrium partition at the entrance and exit on the membrane pore.

Equation (3) is then integrated over the pore cross-section,

$$< J_s >= -K_d D_\infty \frac{d<c>_z}{dz} + K_c < V >< c >_z \qquad (4)$$

Where K_c and K_d refer to the convective and diffusive effects of the transport and are calculated using a relation to λ. Then over the entire membrane length (L) this becomes:

$$< J_s > = \frac{\Phi K_c <V> c_0 [1-\left(\frac{c_L}{c_0}\right)\exp(-Pe)]}{1-\exp(-Pe)} \qquad (5)$$

Pe represents the Peclet number $Pe = \frac{K_c<J_v>L}{K_d \epsilon D_\infty}$, and ϵ is the membrane porosity. The next step is to relate this equation to the rejection defined by $R = 1 - \frac{c_L}{c_0}$. Obtaining the following:

$$R = 1 - \frac{c_L}{c_0} = 1 - \frac{\Phi K_c}{1 - \exp(-Pe)(1 - \Phi K_c)} \quad (6)$$

As mentioned earlier, this relation depends on the permeate flux through the membrane, and the value of λ, which ultimately depends on membrane pore size and solute radius. A further derivation is given in the literature.[14] Hence, for a given membrane pore size, and operating at a specific flux as in the case of this work, we can predict the retention values for a range of molecular weights of compounds or in this case pharmaceuticals. This is assuming however that the mechanism of rejection is mainly steric hindrance. The presented model is discussed and compared to experimental values in the results section.

CHAPTER 3

EXPERIMENTAL PROCEDURE

3.1 Membrane Test Unit and Filtration Protocol

A bench-scale cross-flow membrane filtration system was used to perform all experiments in this study. The system uses a Hydracell M-03 positive displacement diaphragm pump (Wanner Engineering Inc., USA) to deliver feed water from a 25-Liter polypropylene tank to the filtration unit. The commercial membrane cell CF-042D (Sterlitech Corporation, USA) can hold a membrane coupon with an active area of 42 cm^2. Pressure gauges and an in-line temperature sensor were used to constantly monitor the operating conditions. Schematic flow diagram of the bench-scale membrane system is given in the sketch. (Figure 1).

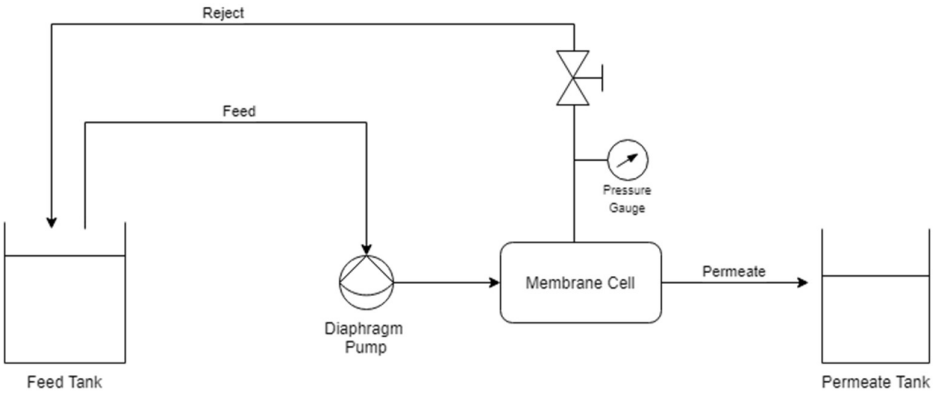


Figure 1: Schematic flow diagram of the bench-scale membrane system

The experiments were carried out in a concentration mode of filtration, in other words the permeate stream was collected separately, while the reject was recycled back

to the feed tank, thus reducing the volume of the feed and increasing the concentration. This filtration mode allows the study of membrane performance as contaminant and salts concentrations increase. In addition to emulating a method used to concentrate contaminant streams in order to more easily dispose of the reject using other techniques like advanced oxidation.[30]

Before every experiment, the membrane coupon was soaked for 24 hours in ultrapure MilliQ water to remove the preservative. The feed water (8L) which also consisted of MilliQ water, prior to spiking it with contaminants and salts, was then heated to 30 ± 0.5 °C and used for a pre-filtration run to measure the pure water permeability of the membrane. The temperature was maintained at a constant value throughout the experiment due to the heat transfer of the pump to the system reaching a steady state equilibrium.

The PhACs were then added to the feed at a concentration of 10 mg/L, first individually each compound was added in addition to NaCl salt at three different concentrations. The salt was added to achieve a TDS concentration of 300, 2000, and 8,000 ppm along with the control run that used distilled MilliQ water and had no salts added. After testing each pharmaceutical individually, a mixture of the three compounds was also used at the different salt concentrations. These experiments were performed for the nanofiltration as well as the reverse osmosis processes.

Pressure was kept constant for the experiments, with nanofiltration (NF) at 130 psi and for reverse osmosis (RO) at 200 psi as per manufacturer recommendations. The feed flow was also kept constant and measured using an F-550 panel mounted flow

meter (Blue-White Industries Ltd., USA). The tangential flow velocity was calculated according to the following equation:[63]

$$Cross\ flow\ velocity\ = \frac{Flow\ Rate}{Chann\quad dept\ \times Channel\ width} = \frac{2.6\frac{L}{min}\times\frac{1\quad m^3}{60000\ \ s}}{0.002\times0.0392} \cong\ 0.5\frac{m}{s}$$

This chosen value is within the operating range of the pump and is comparable to the literature.[64] As for the permeate flux, it was measured by volumetrically collecting an amount of permeate using 25 ml and 10 ml graduated cylinders (ISOLAB Gmbh, Germany) with 95% accuracy, while a stopwatch recorded the time. This method was compared to the electronic balance method, that measures mass rather than volume, and was found to be within 2% of the value.[65] The flux was then calculated using the following equation[66]:

$$J \equiv \frac{1}{A}\frac{dV}{dt}$$

Where J is the permeate flux ($Lm^{-2}h^{-1}$), A is the effective membrane area (m^2), V is the volume of permeate collected (L) and t is the time recorded (hour). Experiments were continued until a volume reduction factor (VRF) of 2 is achieved. In other words, when the feed has been reduced to half of its volume.

$$VRF = \frac{V_i}{V_c}$$

Where V_i and V_c are the initial feed volume and the final volume of the concentrate respectively. During each experiment, samples were collected from the feed and permeate streams and analyzed to measure pharmaceutical concentration, TDS, and

pH. The concentrations of pharmaceuticals were measured in the feed and permeate, C_f and C_p respectively, and then the rejection percentage was calculated accordingly:

$$R\% = (1 - \frac{C_p}{C_f}) \times 100$$

Finally, after each filtration run, the membrane unit was cleaned with acid (HNO3, 0.5%) and caustic (NaOH, 1%) solutions, and then MilliQ water to clear out any residues. The experimental conditions are summarized in the following Table 1:

Table 1: Table summarizing the experimental conditions

Variables		**Operating Parameters**	
Membranes	NF 270 XLE	**Pressure**	130 psi 200 psi
Pharmaceuticals	CBZ – DCF – IBF – Mixture (All 3)	**Cross Flow Velocity**	0.5 m/s
Salt Concentration	Distilled (<50 ppm) 300 ppm 2,000 ppm 8,000 ppm	**Feed Volume**	8 Liters
		Temperature	30 0.5 °C

3.2 Representative Membranes

Two membranes were chosen to represent the nanofiltration and reverse osmosis processes based on their pore size, rejection, and flux values. The NF270 (nanofiltration) and XLE (reverse osmosis) are both manufactured by DOW Filmtec and

were obtained via Sterlitech as flat sheet membrane coupons precisely cut to the respective cell size.

Both membranes are thin film composite membranes, meaning they consist of three layers: a polyester support web, a microporous polysulfone interlayer, and an ultrathin barrier coating on the top surface. The NF270 is a commonly used membrane in industry, usually to treat surface and ground waters. Its active layer is poly-piperazine amide, and it allows for high fluxes and has a medium salt and hardness passage.[67] As for the extra low energy (XLE) RO membrane, it is a common industrial polyamide membrane ideal for a wide variety of applications, like brackish water purification and wastewater treatment.[67] These membranes have been present in multiple publications testing performance, efficiency and mechanisms of removal. [64,68,69] Even though the polymeric makeups of the membranes are given by the manufacturer, the exact composition is unknown, thus multiple characterizations have been made in literature to better understand the membrane properties; they are presented in Table 2.

Table 2: Physiochemical properties of the membranes used in this study adopted from Lin et al.[49]

Property	**NF270**	**XLE**
Membrane Type	Nanofiltration	Low Pressure Reverse Osmosis

Membrane Material	Fully aromatic polyamide TFC	Semiaromatic piperazine-based polyamide TFC
MWCO (Da)	~300	~100
Average Pore Radius (nm)	0.42	-
NaCl Rejection (%)	40%	99%
Zeta Potential (mv) @ pH=7	-21 mV	-33 mV

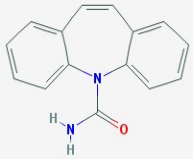
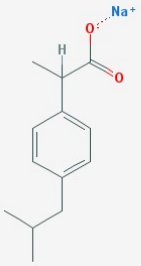
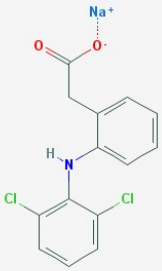
3.3 Representative Pharmaceuticals and Chemicals

The selected pharmaceuticals, carbamazepine (CBZ), ibuprofen (IBF), and diclofenac (DCF), are the compounds within the scope of this investigation. In fact they were selected because they are commonly used and are recognized as priority compounds especially in the developing world, in addition to having an estimated production volume of hundreds of tons annually and potential environmental and health risks.[31,16] CBZ and the sodium forms of IBF and DCF were all obtained from Sigma-Aldrich (Germany). The compound properties are presented in Table 3, and they represent two pharmaceutical classes, different molecular weights, and charges in solution.

The pharmaceuticals were dissolved in deionized water and sonicated to make stock solutions used to spike the feed with pharmaceuticals. The monovalent salt NaCl was obtained from Sigma-Aldrich with >98% purity and was used to mimic the effect of salts on the performance of the membranes. Methanol, Acetonitrile, and Formic Acid

were used as mobile phases for the analytical technique, in addition to the cleaning chemicals sulfuric acid and sodium hydroxide were all also obtained from Sigma-Adrich.

Table 3: The properties of the representative pharmaceutical compounds[70]

PhAC	Carbamazepine (CBZ)	Ibuprofen Sodium (IBF)	Diclofenac Sodium (DCF)
Structure			
Pharmaceutical Class	Anticonvulsant	Analgesic (NSAID)	Analgesic (NSAID)
Molecular Weight	236.2 g/mol	228.267 g/mol	318.129 g/mol
Molecular formula	$C_{15}H_{12}N_2O$	$C_{13}H_{17}NaO_2$	$C_{14}H_{10}Cl_2NNaO_2$
Functional Groups	Carboxamide, Dibenzazepine derivative	Carboxylic Acid	Carboxylic Acid
Log Kow	2.45	4.51	3.97
Charge in Solution	Neutral	Negative	Negative

3.4 Analysis

Samples taken from the experiment were analyzed on the spot for conductivity and pH using a EUTECH CON11 conductivity meter from Thermo-Scientific, and a benchtop pH meter from Mettler-Toledo, respectively. Then the samples were placed in 2 mL vials for further pharmaceutical concentration analysis.

A High-Performance Liquid Chromatography (HPLC) system was used to determine the concentration of pharmaceuticals in solution. The HPLC system used the Agilent 1100Series LC system, equipped with a quaternary pump, an autosampler, and a diode array detector (DAD), and supported by an analytical work station all supplied by Agilent Technologies (California, USA). The pharmaceuticals were separated using a reversed phase Supelco Discovery HS C-18 (5mm, 25cm x 4mm ID) column along with a connected guard column (5mm, 2cmx4mm ID) both obtained from Sigma-Aldrich. Analytical calibration curves were constructed from prepared internal standards using the stock solutions with concentrations ranging from 1-15 mg/L. The methods used to test for the concentrations were adopted from previous studies and are available in Table A1 in the Appendix.[71]

CHAPTER 4

RESULTS AND DISCUSSION

4.1 Nanofiltration

4.1.1 Rejections of Individual Pharmaceuticals in Distilled Water

The results obtained from the nanofiltration experiments showed moderate rejection values for ibuprofen (IBF) and carbamazepine (CBZ), while high rejection was shown for diclofenac (DCF). The rejection values for the pharmaceutical compounds in distilled water with the NF270 membrane are given in Figure 2. As mentioned in the transport theory section, the steric hindrance effect is the dominant rejection mechanism for organic compounds like pharmaceuticals. The largest compound used was DCF with a molecular weight (MW) of 318 g/mol, well above the MWCO of NF270, and relatively large compounds like this one are expected to be rejected efficiently. Indeed, it can be seen that DCF had a consistently high rejection throughout the experiment, in addition to the hydrodynamic model predicting this high rejection.

As for IBF, it is the molecule with the lowest MW out of the three pharmaceuticals, and it is negatively charged at neutral pH. The role of electrostatic effects is more prominent when the compound has a MW less than or within close range of the membrane MWCO.[40] Some studies showed that when eliminating the electrostatic effect by changing the pH and thus uncharging the compound or the membrane, it can be seen that ibuprofen rejection decreased. Looking at Table 4, the

mass balance for IBF in the NF experiment, almost 5% of the starting amount was found to be adsorbed on the membrane. Thus, we can deduce that size exclusion, electrostatic repulsion, and to a lesser extent adsorption are all rejecting the compound in this system.[72]

Table 4: Mass balance for IBF with NF270 in distilled water

IN		**OUT**			
Vol Feed (L)	Conc Feed (mg/L)	Vol Permeate (L)	Conc Permeate (mg/L)	Vol End	Conc End
8	9.78	4	1.91	4	16.56
IN= Vf* Cf		OUT = Vp*Cp + Ve*Ce			**% Adsorbed**
78.24		73.88			**5.57%**

CBZ has a dissociation constant (pK_a) value of 2.3, this means it is a neutral organic solute when in solution, hence electrostatic effects are not expected to play a role when considering the rejection mechanisms. Having a molecular weight close to the MWCO of the NF270 membrane, and a log K_{ow} of 2.45, therefore steric hindrance and hydrophobic interactions will both influence the rejection of the compound. The initial increase in the rejection of CBZ could be attributed to the progressive adsorption of the compound on the surface of the membrane till it reached equilibrium and stabilized at around 77% rejection. It is likely that CBZ would adsorb on to the surface of the membrane and the pores using a hydrogen bond. The adsorption of CBZ on the NF270 membrane has been documented and it could lead to the overestimation of its rejection, due to the high concentration used in these experiments the membrane is expected to be saturated with CBZ within the first few minutes of the experiment.[68] In

fact mass balance calculations (Table 5) on the system showed that around 10% was adsorbed on the membrane.

Table 5: Mass balance for CBZ with NF270 in distilled water

IN		**OUT**			
Vol Feed (L)	Conc Feed (mg/L)	Vol Permeate (L)	Conc Permeate mg/L	Vol End (L)	Conc End (mg/L)
8	10.05	4	2.02	4	16.05
IN= Vf* Cf		OUT = Vp*Cp + Ve*Ce			**% Adsorbed**
80.432		72.108			**10.35%**

Figure 2 shows the rejection of the pharmaceuticals individually by nanofiltration in distilled water. Due to time and resource constraints, the error bars represent a percentage error based on one repeated experiment for each pharmaceutical and represent around 1-3% error. For the rest of the results, experiments were not repeated, hence error bars were excluded. Further research will include repeated experiments with standard deviations.

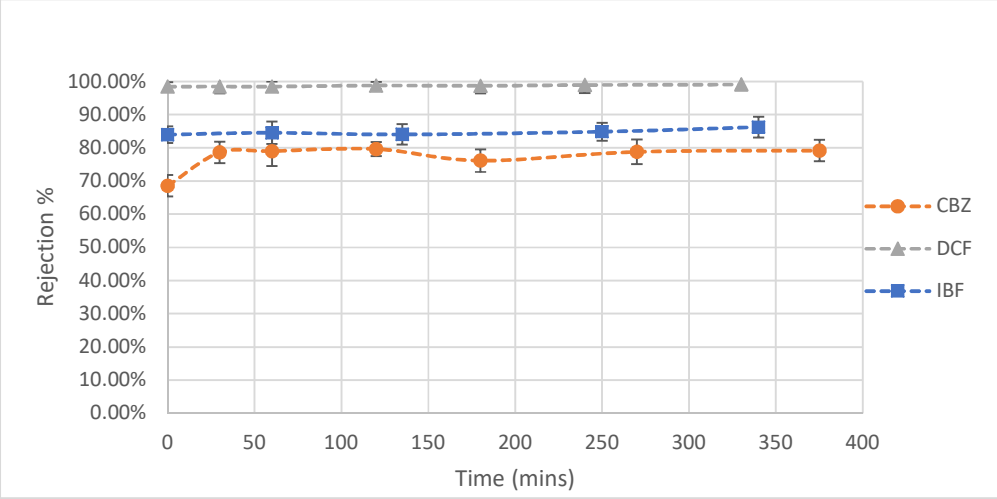


Figure 2: Rejection values for the pharmaceuticals in distilled water with NF270 taken at different times throughout the experiment

4.1.2 Model

Figure 3 shows the model applied to the NF270 membrane which was used in this research at an approximately similar operating flux.

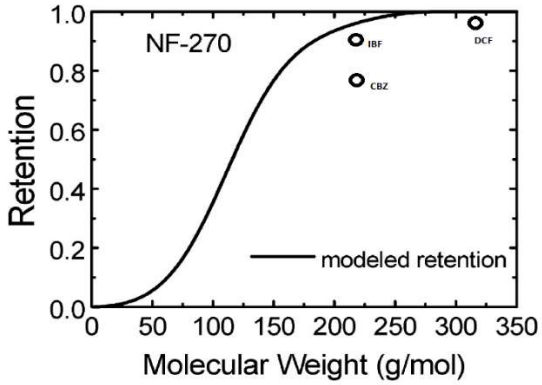


Figure 3: Model prediction for the retention of organic compounds for the NF270 membrane as a function of molecular weight based on the pore transport model Adopted from Nghiem et al.[14] Experimental retentions were also included at distilled water condition.

The experimental results of the rejection are also shown in Figure 3, in relation to the model and it seems to almost predict the cases of Ibuprofen and Diclofenac and overpredict Carbamazepine. Ibuprofen has a charged character which should be causing its good rejection values, whereas Carbamazepine's hydrophobic character adds to its partitioning and diffusion into the permeate, and Diclofenac's high relative molecular weight ensures its rejection by size exclusion. This is discussed further in the results section. It is important to mention that the operating temperature was a little higher than room temperature which could affect the results. As for the XLE RO membrane, the pore size is relatively small enough that all the compounds are expected to be rejected fully at 100%.

4.1.3 Distilled Individual Rejection vs Pharmaceutical Mixture

After studying the rejection rates individually for each pharmaceutical in distilled water using the nanofiltration NF270 membrane, the effects of a pharmaceutical mixture were then studied by including all three compounds in the feed and observing whether a change arises in the rejection values. The results are presented in Figure 4.

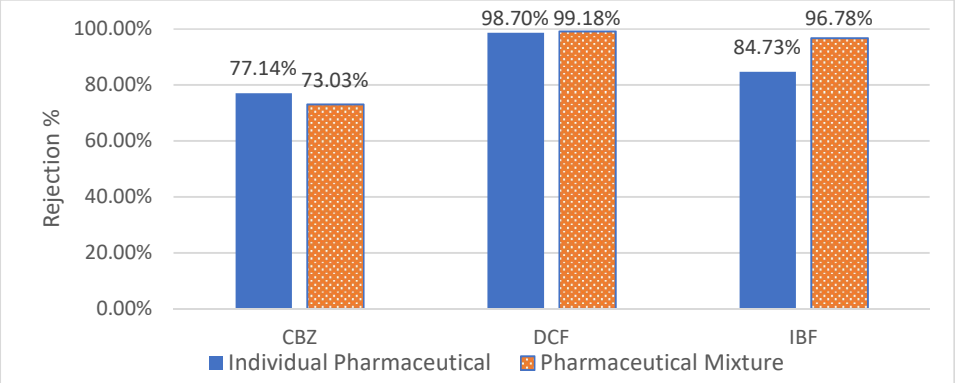


Figure 4: Rejection values for the pharmaceuticals averaged over the experiment run time; individually vs mixture

DCF rejection was not affected by the addition of other pharmaceuticals, confirming that size exclusion governed its rejection and that it was not influenced by the PhAC mixture effect. The uncharged compound CBZ however, showed a slight decrease in rejection (4%) when it was introduced to the pharmaceutical mixture with the other compounds. IBF rejection was enhanced significantly (increase of 11%) when mixed in with the other pharmaceuticals. These effects are not fully understood and could be attributed to several mechanisms.

Competitive adsorption could explain the decrease in CBZ rejection as the molecule has been shown to adsorb on the NF270 membrane surface, and having another component competing for that adsorption site could allow for the transfer of the molecules into the permeate. Competitive adsorption has been reported in previous literature, where ibuprofen showed to compete for membrane active sites against another pharmaceutical in static adsorption experiments. However, the repulsion effect was neglected in the experiment because it had occurred at a low pH.[49,68]

Another possible explanation is an increased effective pore size, as explained in the transport theory section, this phenomenon has been predicted by models, where the concentration of ions on the membrane surface increases and so the membrane charge increases, causing a higher repulsion between the pores, thus decreasing the rejection for neutral solutes.[50] However, for this to be true, we have to assume that the change in pore size did not affect the other two pharmaceuticals DCF and IBF since they are charged compounds, so their rejection would have to be attributed to a larger extent to electrostatic repulsion to compensate for the increased pore size.

The latter theory would also explain the high increase in IBF rejection, as the charged DCF molecules, too large to permeate and possible to adsorb on the membrane, could have helped increase the membrane charge enough to aid the repulsion of IBF. The question remains however if having a small amount (10 mg/L) of DCF is enough to elicit such an effect.

4.1.4 Effect of Salt on Nanofiltration

Foulants like organic matter and inorganic compounds can be removed in various ways and combining processes is often the case when using membranes. NaCl was used as the model monovalent salt as it is the most abundant in most desalination settings. Indeed, it is a difficult task to assess the situation and tell for sure which mechanism is playing the largest role and how it is being affected by the salt. Nevertheless, speculations are made with reference to previous literature in order to have a better understanding of these effects.

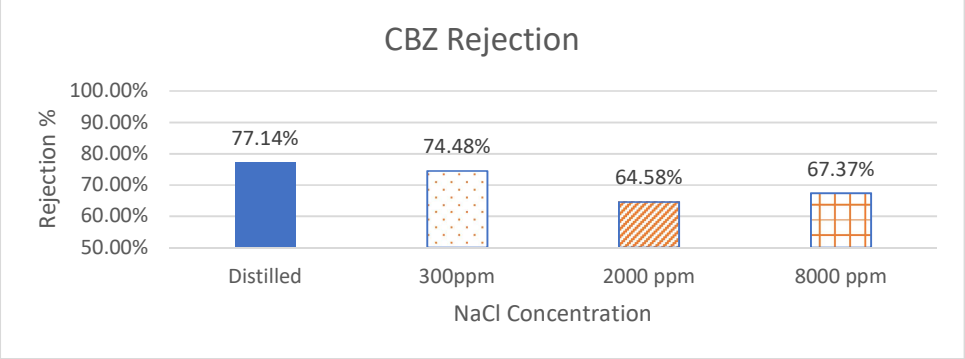


Figure 5: Rejection values for carbamazepine, averaged over time, at different NaCl concentrations

Salt has been known to affect neutral organic solute rejection negatively, for example Bargeman et al. found a pore distribution exists within the membrane and that the presence of salt in the pores reduces the flux through the small pores more than the larger ones. It was hypothesized that the drop in glucose retention happens due to this phenomenon and this was supported by Maxwell-Stefan model calculations.[50] Whereas Escoda et al. attributed the drop in polyethylene glycol retention to pore swelling effects on the membrane along with the salting-out of the molecule, and had confirmed using charge density and effective size calculations.[51]

Figure 5 shows the average rejection values for the nanofiltration of CBZ with NF270 at distilled water and at the 3 different salt concentrations. A decrease in the rejection of CBZ is observed with the increase of NaCl concentration, till the 8,000 ppm mark where a slight increase is shown. The results agree with the literature regarding the effects of salts in the nanofiltration of neutral organic solutes. Two mechanisms might be simultaneously responsible for the drop in rejection rates, including the pore swelling effect as reported and the salting-out effect. CBZ has a low solubility in water, and adding salt to the mixture could very well cause its effective hydrated radius to decrease making it more likely for the molecule to permeate the membrane. Both these mechanisms increase in significance with increasing salt concentrations, however the threshold seems to point out that another effect occurs at high concentrations. Looking at the flux variations throughout the experiments could give more insight to the process.

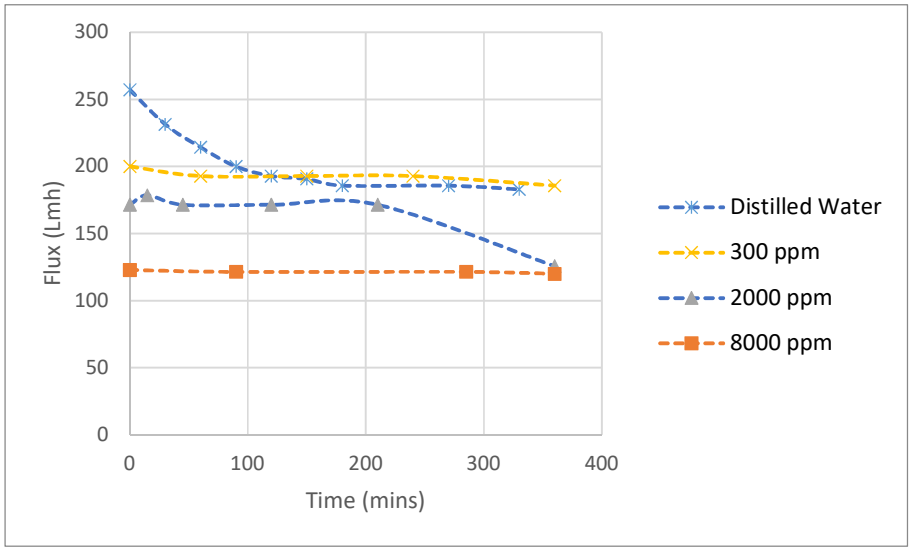


Figure 6: Flux values for CBZ filtration at different NaCl concentrations

The flux values given in Figure 6 show a decreasing trend as the salt concentration increases. It is interesting to note that the flux dip at the start of the

distilled water experiments coincides with the rejection rise in Figure 2 for CBZ. This shows that the molecules need around 30 minutes to reach equilibrium on the membrane surface. Comparing flux values at 8000 ppm to the flux with pure water, it decreases to around half of its original value. The higher volume of salt ions adsorbed on the membrane could slightly restrict the pores causing a flux decline and hindering the transport of CBZ through the membrane. This would explain the slight increase in rejection values at the 8000 ppm mark. It is interesting to note that this effect of NaCl on CBZ and the increase noted at the high concentration has been reported in literature and was attributed to the dehydration of the CBZ molecule allowing it to pass through the membrane more easily.[32]

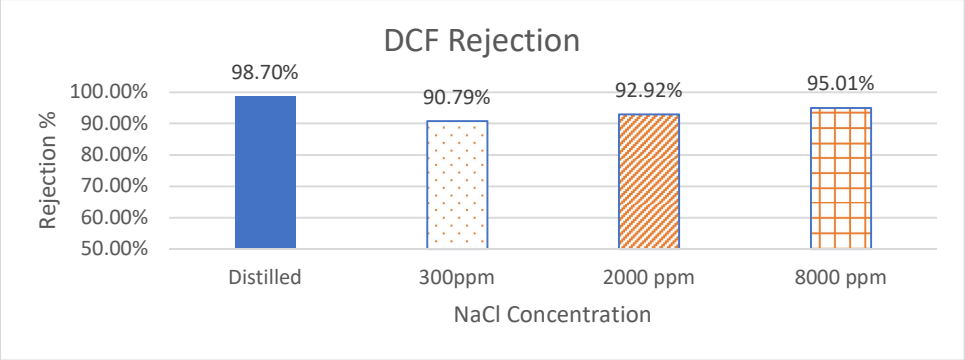


Figure 7: Rejection values for diclofenac (DCF), averaged over time, at different NaCl concentrations

Alternatively, the high molecular weight of DCF and its negative charge had given the compound high rejection values when in distilled water. However, upon the addition of a low concentration of salt a drop of 8% was observed in its rejection. Yet the subsequent addition of more salts caused an increase in rejection. Figure 7 shows this effect at the three different experimental conditions. This case could be justified by the pore swelling phenomenon, as the addition of a low amount of salt (300 mg/L)

could be enough for ion adsorption in the membrane pores and cause some repulsive forces inside the pores allowing them to swell. Upon increasing this concentration, it is speculated that a concentration gradient develops insides the pores causing the DCF molecules to also adsorb in the pores, however due to its size this could impact the pore size negatively causing a shrinkage or blockage of the pore resulting in a better rejection. Modeling the parameters and deducing the pore size from these experiments could prove useful to figuring out if this proposed mechanism is likely to happen.

Another explanation could be the polarizing effect, i.e. the salt could change the orientation of the molecule and its dipole moment. This can result in its easier transfer through the membrane. However, this effect will have to become less pronounced as the concentration increases. Similarly, the "salting out" dehydration effect is probably not the case because one would expect a further decrease in rejection as concentration increases if that is the mechanism.

Furthermore, Figure 8 shows the effect of increasing salt concentration on DCF rejection during each experiment. The NF270 rejects NaCl at around 40%, and since the process is operated in concentration mode, this means that the salt concentration increases as the experiment progresses. For the 300 ppm concentration experiment (represented by ▲), the DCF rejection was at 88%; as the experiment ends we can see that the salt concentration increases to 550 ppm (or 0.55 g/L), and DCF rejection value also increased to 92%. The same trend can be seen at higher concentrations, suggesting a possible positive relation between salt concentration and DCF rejection, when not considering the distilled water case. This shows that it is not only the average rejection value that is affected by the salts but also the instantaneous rejections during the

experiment. It would be interesting to see if the trend continues in this fashion, or if a threshold will result in a decreasing slope. This effect was not seen on the other pharmaceuticals.

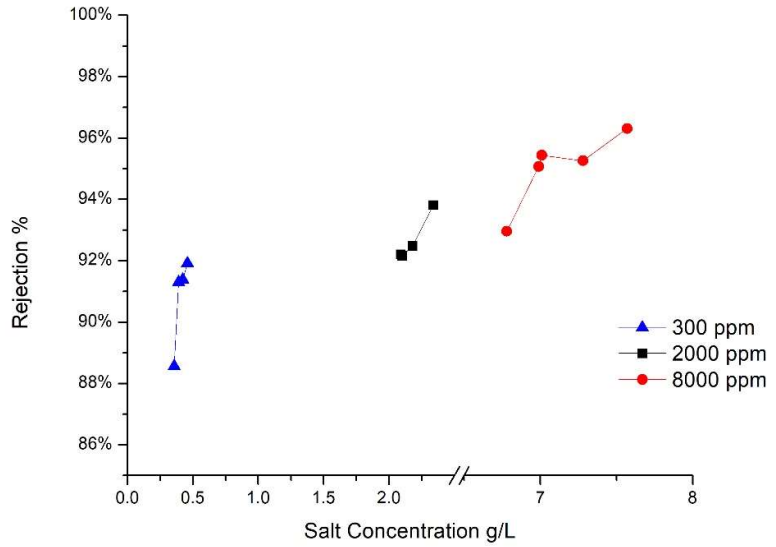


Figure 8: Instantaneous rejection values for diclofenac (DCF) vs salt concentrations for 3 different experiments

Interestingly, an increase in IBF rejection is observed when NaCl salt is added. Figure 9 shows an increase of 11% in the average rejection values as the salt concentrations are increased, until at the concentration of 8,000 ppm NaCl where the rejection drops, however still performing better than when no salts were added. Enhanced rejection for membrane processes when adding salt is not a usual phenomenon, since as discussed, salts more often cause reduction in rejection, flux, and overall performance of the membrane. The following explanations will try to make sense of this result and understand the mechanism playing a role in this increase of retention.

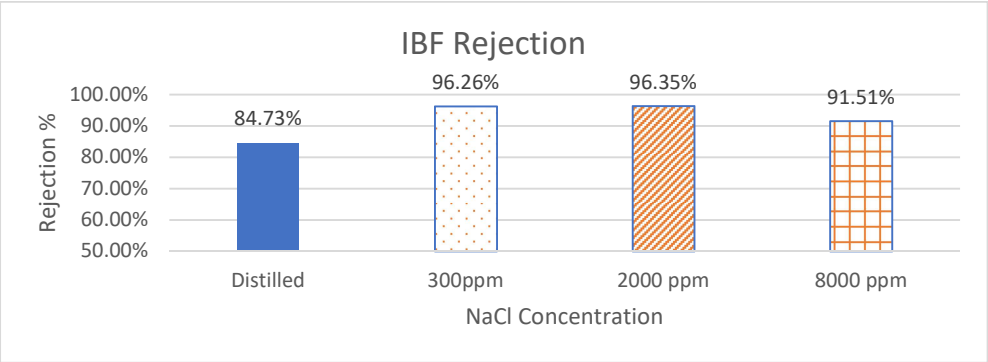


Figure 9: Rejection values for ibuprofen (IBF), averaged over time, at different NaCl concentrations

An increase in ionic strength of the feed solution decreases the effective charge density of the membrane, and this allows the passage of more cations to the permeate side. This creates a charge imbalance and demands anions to permeate through the membrane to maintain electroneutrality of the solution thus causing a competition between the anions. This result was present in a study where the effect of ammonium salts on the nanofiltration of the amino acid glutamate was discussed, and an increase in the rejection of the solute was reported. This increase is attributed to co-ions competition, and in this case, it represents the competitive transmission of chloride ions to the permeate since Cl^- has higher mobility and less charge than the glutamate amino acid, hence increasing the rejection of the solute.[73]

When the salt effect on glucose was studied as mentioned above, Bargeman et al. also found a high concentration of Cl^- in the permeate due to the pore size distribution and selectivity of the membrane in high ionic strength situations, and this high concentration coincided with a high rejection of glucose, further solidifying the

claim.[50] In fact IBF rejection in nanofiltration was reported to increase with increasing NaCl concentration recently.[27] The drop in rejection was also observed at around 5,000 ppm; this means there is a threshold where either the positive effect of the salt on rejection starts to become less significant or another negative effect starts to counteract the former. The mechanism, reported by the author, that was responsible for this increase in rejection was anion competition. Chloride ions have a higher diffusivity than IBF molecules, thus allowing their transport through the membrane more easily.. The results presented in Figure 9 can be explained by this co-ion competitive mechanism as well.

However, in another study an enhanced rejection of pesticides was reported in tap water vs distilled water. The reasoning behind the results was the interactions of ions and the membrane. The ions in tap water adsorb on the membrane surface or inside the pores, thus the pores become narrower and pesticides are rejected more efficiently.[74] Even though this is not in accordance with the pore swelling theory, which speculates that adsorbed ions cause repulsive forces that increase the membrane pore size, however it is possible that these ions along with the large pesticide molecules could cause pore narrowing.

The threshold observed could be the result of a either pore swelling starting to take effect due to the high volume of ions adsorbed on the membrane or a balanced electroneutrality. IBF would no longer have a disadvantage to permeate the membrane at this balanced point, however the rejection still seems to be better at this point rather than with the distilled water. This threshold can also be due to the dehydration effect and further experiments at higher concentration could help make this clearer.

4.1.5 Combined PhAC mixture and Salt Effects

Finally, the effect of salts on the pharmaceutical mixture was studied by combining the three pharmaceuticals and adding the same concentrations of salt as previously added, and this can help clarify if a combined effect can occur. The results are presented in Figure 10 The same patterns of rejection seem to be present here as in the effect of the salt alone on the pharmaceuticals, except for CBZ as it seems to have an opposite effect completely in this case and is worth investigating further.

As for DCF, high rejection values (>95%) were found again, since it is a relatively large compound steric hindrance seems to be responsible for these high rejections. The effect of the PhAC mixture reduced the magnitude of the effect the salt had alone previously. This could be due to the narrowing effect that was hypothesized (speculated) whereby the compounds adsorb to the charges on the cations that are adsorbed on the pores.

IBF showed the same pattern as previously discussed, with the highest rejection values peaking at 2000 ppm of NaCl concentration. It is interesting to note that IBF still maintained the lowest rejection when it was in distilled water without any other components. The combined effect of the pharmaceutical mixture and salt did not differ in results compared to their respective individual effects. The same speculations as noted in section 3 apply in this case as well.

The increase in CBZ rejection can also be attributed to the pore narrowing effect noted earlier. One would expect this effect to only increase as the concentration increased as well, however, a dip in rejection occurs at the 8,000 ppm mark and this is

in fact the opposite of what occurred with CBZ at the same threshold with NaCl without the rest of the pharmaceuticals. Once again two speculations could be made for this case: the sudden drop in rejection is due to the pore adsorbing to many charged components causing a repulsive pore swelling mechanism to overpower the "pore narrowing" and allow the CBZ to pass through more easily to the permeate. Another explanation could be the saturation of the membrane with enough CBZ molecules till the subsequent diffusion of CBZ through this layer occurs and results in lower rejection values. The latter phenomenon has been reported, however it was reported to happen at the start of the experiment and regardless of the salt concentration or whether any other components affected the process.[68]

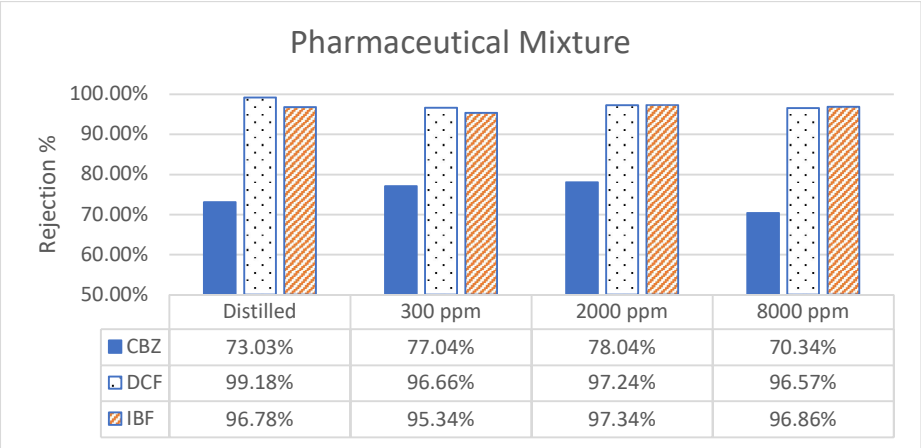


Figure 10: Average rejection values for the three pharmaceuticals with the combined PhAC mixture and salts effects with NF270

4.2 Reverse Osmosis

4.2.1 Distilled Individual Rejection vs. Pharmaceutical Mixture

The XLE membrane proved to be very efficient at rejecting pharmaceuticals as expected. The low MWCO of the membrane (~100 Da) is a good indicator of what to expect when dealing with organic solutes like the pharmaceuticals with molecular weights well above this value. The results for rejection in distilled water and in the PhAC mixture, presented in Figure 11, showed that the compounds were efficiently rejected, at least to the limits of detection of the analytical method (50 µg/L).

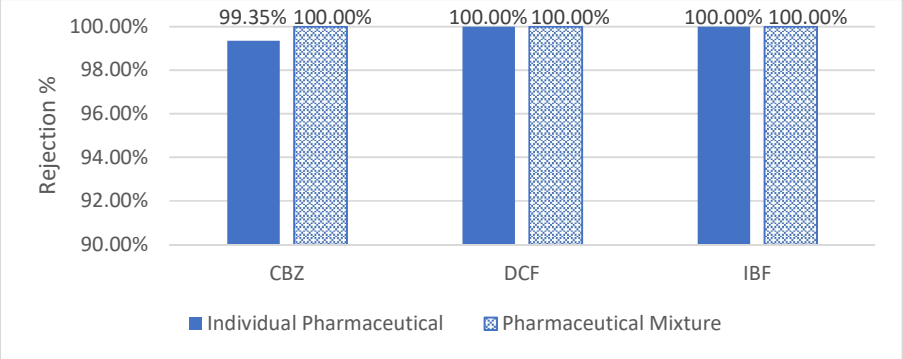


Figure 11: Rejection values with the XLE membrane, averaged over time, in distilled water

The results agree with most reported literature using the XLE membrane. Kimura found very low traces (ppb levels) in the permeate after filtering surrogate compounds representing pharmaceuticals, and also attributed the rejection to the low MWCO of the membrane.[41] Indeed, high rejections of pharmaceuticals were reported by others using this same membrane.[75] A sieving effect must have been responsible for this efficient retention of the pharmaceuticals because of the relative high molecular weight

of the compounds in question compared to the pore size of the membrane, represented by the MWCO.

4.2.2 Salt Effects

The addition of NaCl to the feed at different concentrations did not have much of an effect on the rejection values for each pharmaceutical. As shown in Figure 12, the largest variation was a 2% change in retention which cannot be considered as a significant effect.

These results agree with what has been reported, as the XLE membrane was tested under different water matrices in the literature, and it was also seen to have good rejection values for pharmaceuticals irrespective of the matrix.[32] Rejection of pharmaceuticals using RO membranes seem to remain unchanged regardless of the ionic strength due to the presence of salts or even other pharmaceuticals as seen earlier in Figure 11.

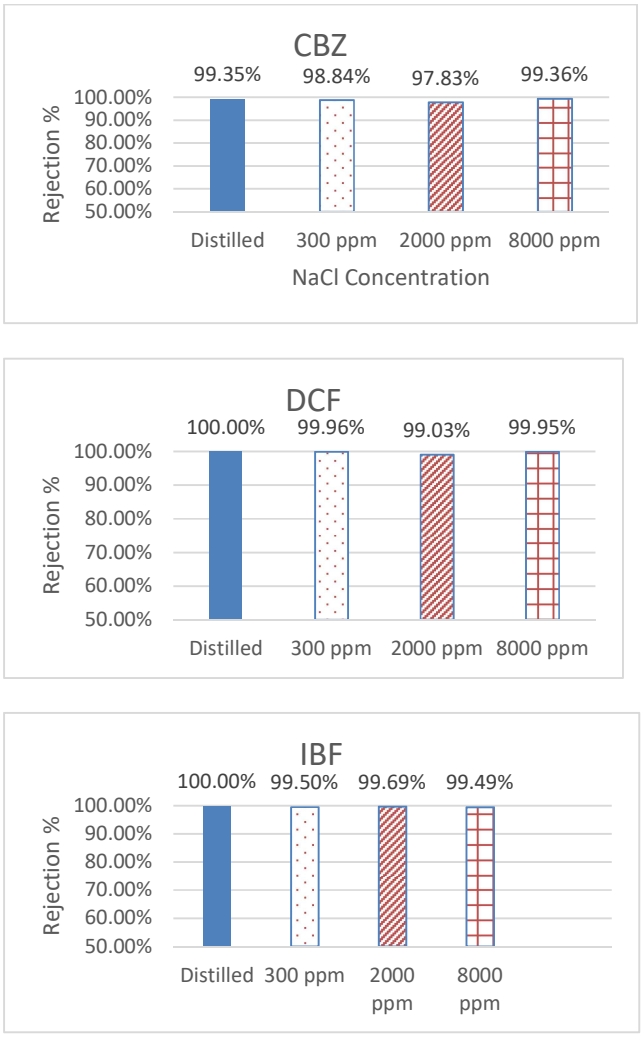


Figure 12: Rejection values for each of the pharmaceuticals (CBZ, DCF, and IBF), averaged over time, at different NaCl concentrations with XLE membrane

Even though the rejection values were unaffected, NaCl concentration did indeed have a negative effect on the flux of the permeate. Similar to the case seen with NF (Figure 6), the permeate flux decreased as the experiment went on since the setup is run in a concentration mode of filtration and feed concentration is expected to increase, in addition the flux also decreased substantially as the salt concentration increased. This decrease in flux is expected and does not necessarily mean it would affect the rejection values. The increase in salt concentration causes an increase in osmotic pressure, and

since the operating pressure was kept constant the flux will suffer and decrease as shown in Figure 13.[76]

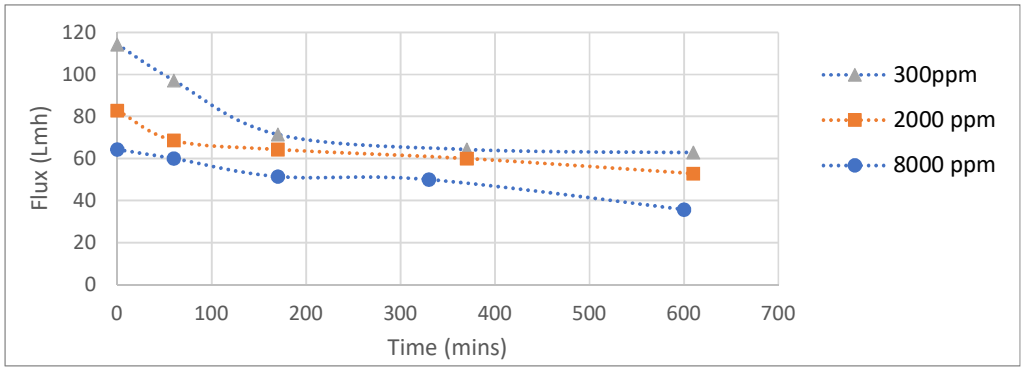
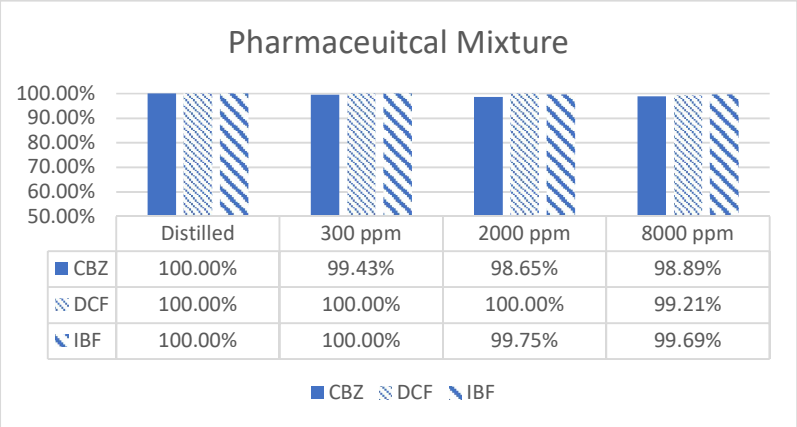


Figure 13: Flux values for the CBZ experiments with XLE membrane at different salt concentrations

Flux decline is different from fouling which usually leads to the reduction of rejection values however in this case the decline just increased experiment time making the process less efficient in total. Fouling due to organic matter or divalent salts, its mechanisms and its effect on perfermance are out of the scope of this study.

4.2.3 Combined Pharmaceutical Mixture and Salt Effects



	Distilled	300 ppm	2000 ppm	8000 ppm
CBZ	100.00%	99.43%	98.65%	98.89%
DCF	100.00%	100.00%	100.00%	99.21%
IBF	100.00%	100.00%	99.75%	99.69%

Figure 14: Average rejection values for the three pharmaceuticals with the combined mixture and salts effects with XLE

Contrary to the NF results again, the XLE membrane was efficient in rejecting the pharmaceuticals even with the combined effect of salt and the pharmaceutical mixture. The variations are once more too miniscule to be of significance but is only proof of some traces of pharmaceuticals making their way into the permeate. The individual salt effect and the mixture effect did not influence the rejection, so the results presented in Figure 14 affirm that the combined effect of both would not influence rejection values or mechanisms either.

4.3 Comparing NF vs RO

The NF and RO membranes used in this study are manufactured from similar materials, and possess similar charges in solution, yet have different pore sizes. The RO membrane's pores are much smaller and is sometimes considered not to have pores at all. The fact that this monovalent salt was not able to affect the rejection of RO but did

indeed affect NF rejection could point to the fact that the salt interferes with pore size using mechanisms like swelling and narrowing.

In addition, the RO experiments although performing better as rejection values, had much lower flux rates and hence needed longer running times. It is important to note that even though the XLE membrane showed better rejections, one needs to consider other process parameters. For example, how quickly the membrane fouls due to contaminants in the feed, called propensity of fouling. While monovalent salts do not affect this aspect, organic matter and large inorganic salts do in fact cause the membrane to foul and be no longer functional in terms of flux decline and rejection values.

NF270 showed 2-2.5 times as much permeate flux rate especially at high salt concentrations and at a lower pressure at that. Cleaning the membrane is also easier due to the larger pores and lower operating pressures, thus saving on membrane replacement costs. In fact, in an economic analysis comparing NF270 with an RO membrane done by Bellona et al. it was shown that using NF would result in savings of $55,000/year on a 425 m^3/h production. The study took into account the higher flux values and membrane cleaning and replacement costs. It was noted however that the lower rejection values might need additional steps in order to meet required guidelines.[77]

Until nanofiltration becomes more popular and more efficient at removing contaminants, a low energy reverse osmosis process could be the better solution. Understanding the mechanisms and the properties that affect them is key to optimizing the process and making better membranes that could withstand different challenges.

4.4 SEM Images

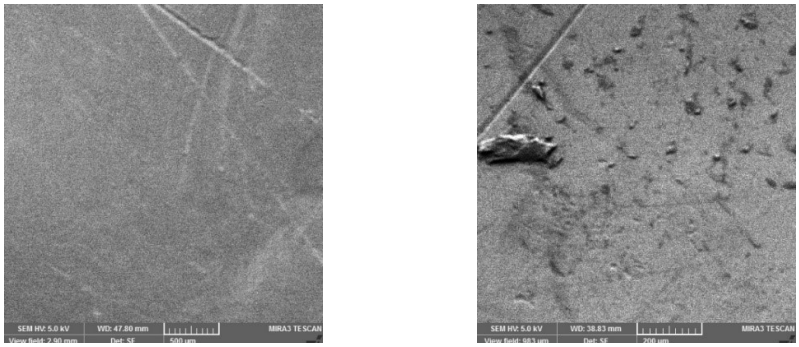


Figure 15: Virgin NF270 (left) vs NF270 after filtration of pharmaceutical mixture at 2000 ppm (right)

The SEM images of the membrane surfaces cannot give much information about the pore size as the pores are theoretically at the 10^{-1} nm scale which is below the resolution of the SEM. The XLE membrane seems to have a smoother surface at the reported magnification. The images do show however that salt and what is presumed to be pharmaceutical particles adsorb and deposit on the surface of the membrane. This means that these contaminants might eventually cause fouling in the membrane if not cleaned properly.

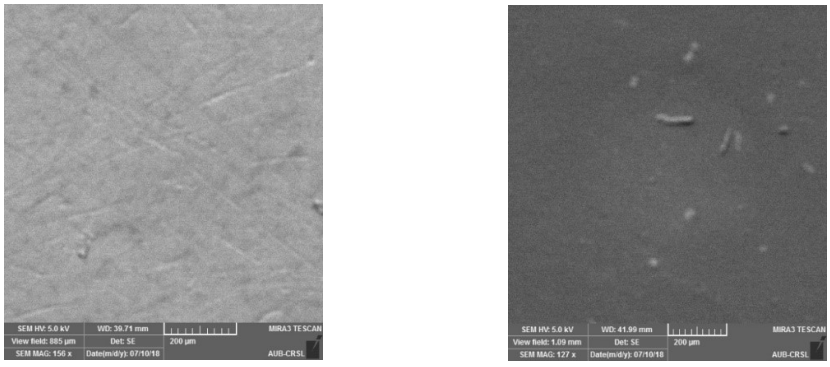


Figure 16:Virgin XLE (Left) vs XLE after filtration of pharmaceutical mixture at 2000 ppm (right)

CHAPTER 5

CONCLUSION

In this work, a bench-scale membrane system was used to evaluate the removal of three pharmaceuticals by two types of membranes at different salt concentrations. The rejection values in distilled water for the nanofiltration of CBZ, DCF, and IBF were 77%, 98% and 85% respectively, whereas removal rates >99% were found for the tighter reverse osmosis membrane. The mechanisms responsible for these values were suggested and explained, and the values were compared to a hydrodynamic model based on steric effects. It was also found that the interference of a mixture of pharmaceuticals had an effect on the smaller compounds, CBZ and IBF, decreasing the retention of the former and increasing the rejection values of the latter.

The effect of the salt NaCl on the filtration of the pharmaceuticals was found to be dependent on the compound properties and the membrane type. For nanofiltration, the salt enhanced the retention of the charged compound IBF and decreased the values for CBZ and DCF. The experimental results also revealed a threshold at 8000 ppm where properties start to change for IBF and CBZ. As for reverse osmosis, the salt did not have any significant effect on the retention of the pharmaceuticals but did influence the flux, diminishing it to around half its value. Speculations on the molecular mechanisms that played a role in these influences were made while referring to the literature. Future studies with a larger scope could see more patterns emerge to solidify speculations and help in a better understanding of these processes. For example, studying higher concentrations of salts is essential to understanding the salt effect and how far this influence can affect the process, in addition to looking at divalent salts and

how that differs from the effects mentioned in this work. The investigation of other factors, such as temperature and pH, is also recommended in order to get a more complete picture of the process. Finally, with the information presented above in addition to other studies, further research could prove successful in finding mathematical models to better predict the removal of pharmaceuticals from water using membrane processes.

APPENDIX

Table A1: HPLC Methods for the concerned pharmaceuticals adapted from Baalbaki et al.[71]

Name of Pharmaceutical	Eluent	Elution mode	Flow rate (mL/min)	Injection volume (µL)	Column temperature (°C)	Detection wavelength (nm)	Retention time (min)
DCF	mixture of MeOH/0.1% formic acid in water (80:20, v/v)	isocratic mode	1	25	30	275	7.24
IBU	(Acetonitrile) ACN/0.1% formic acid in water (65:35, v/v)	isocratic mode	1	50	30	196	8.3
CBZ	MeOH/0.1% formic acid water (70:30, v/v)	isocratic mode	0.8	30	30	235	5.98

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