### Diffusion of fluoxetine through a reverse osmosis membrane

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#### ABSTRACT

The antidepressant, fluoxetine (FLU), often contaminates water resources because of its high solubility and persistence. Reverse osmosis appears to be a promising and effective technique for its removal. However, it is necessary to understand the mechanisms of the transportation of the solute and solvent for applying the method so as to ensure adequate yield. This study aims to evaluate reverse osmosis as an advanced technique for the removal of FLU from water, using a solution–diffusion model to describe and understand the separation and mass transfer across the membrane. The high removal rate of the drug (>99%) under the tested conditions stands out, even for different pressures and concentrations of the FLU at controlled temperatures and pH values. The solution–diffusion model was able to justify the interaction between FLU and the polyamide layer, with the effective diffusivity of water being 250 times higher than that of the FLU.

Keywords: Micropollutants; Water treatment; Solution-diffusion; Diffusivity; Emerging pollutants

#### 1. Introduction

The presence of micropollutants such as pesticides, hormones, and pharmaceutical compounds is often detected in the environment. These micro-pollutants are found in small concentrations as free compounds and/or as metabolites in different sources across the world, including drinking water, wastewater effluents, soil, and sediments [1–7]. However, even at low concentrations, these compounds can pose a risk to aquatic ecosystems as they can cause changes in the bodies of organisms including humans [8–11]. Among the many classes of pharmaceutical pollutants, this study focuses on antidepressants. The use of antidepressants is increasing each year and in ever-lower age groups [12–14]. Fluoxetine (FLU) (under the tradename Prozac®) acts by selectively inhibiting serotonin uptake, resulting in desired effects on the patient. It is a psychoactive drug widely used in the treatment of depression, anxiety, and lack of appetite control [12,15,16] and is detected in the environment at trace levels in ranges between ng L<sup>-1</sup> and  $\mu$ g L<sup>-1</sup> [17]. Synergistic, addictive effects or accumulation may occur. In addition, FLU has been reported to be one of the most persistent pharmaceutical products in the selective serotonin replenishment inhibitors group, even after treatment [12,14,18]. Their excessive consumption, whether licit or otherwise, is a matter of concern for health

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and safety authorities and can be considered an environmental issue that has a bearing on sustainable development.

Water and wastewater treatment methods are not designed to eliminate most emerging pollutants, usually due to their persistence in water environments. Thus, complementary processes are required to remove these compounds. The lack of adequate toxicological data on chronic exposure and toxicity recommends the total elimination of any type of micropollutants from drinking water.

Membrane separation processes can be an option for the advanced treatment of water, but they need to be investigated as they are still considered unusual in these systems [6,11,19]. Reverse osmosis (RO) allows the use of treated water for other purposes, demonstrating an efficient method for the removal of various emerging contaminants [5,19-21]. Reverse osmosis is recognized as the technology that offers the best and most cost-effective process option available today [3,7,22,23]. However, the membrane used in the process is not a perfect barrier. In general, a hydrophobic selective layer facilitates the adsorption and transport of organic solutes, which often results in inadequate removal of pesticides, pharmaceuticals, and endocrine-disrupting compounds, and limits their practical use [24]. Knowing the mechanisms of solute and solvent transport across the membrane allows us to choose a suitable membrane for each application or even to develop new, more efficient separation membranes.

Transport models are the tools used to understand permeation through the membrane. Two primary categories exist: phenomenological and mechanistic. The classical Kedem-Katchalski model is a phenomenological model, where the membrane is considered a "black box" and slow processes occur in near-equilibrium conditions. However, solution-diffusion is a mechanistic model. It has been developed to describe the mass transfer in a membrane taking into consideration the physical (pore structure, solute size) and chemical properties (energy of interaction) of the membrane and solute materials. Such structure-performance relationships allow for a more fundamental understanding of membrane transport [25,26]. Both models are used to describe the permeation through reverse osmosis membranes, helping to predict the permeation of solvent and solute and the separation performance of micropollutants.

The removal of pharmaceutical micropollutants by polymeric membranes has been investigated by the scientific community. Reverse osmosis can remove several pharmaceutical compounds at rates higher than 75% and are less influenced by effects such as electrostatic and hydrophobic interactions than NF membranes [4,48]. The studies focused on high-rejection-RO membranes [4,11] with lower flux and higher energy consumption than ultra-low pressure (ULP) RO membranes. Ultra-low-pressure reverse osmosis has been shown to be an efficient technique for the treatment of potable water or wastewater, contributing to water quality and public health. These membranes could be used by individual households to remove traces of pharmaceuticals in drinking water. Some studies have shown that low-pressure RO membranes can remove pharmaceuticals from water [19], and these pharmaceuticals can adsorb on the polyamide layer [36]. The solutiondiffusion model has been shown to be a good model for

representing the transport of uncharged organics in ionexchange membranes [45], but the mechanism of transport of FLU (a neutrally charged pharmaceutical) through hydrophobic uncharged ULP RO membranes is to be explored and holds promise in achieving better removal rates.

The aim of this study is to evaluate reverse osmosis as an advanced technique to remove fluoxetine from water and investigate the diffusion to describe and understand the separation and mass transfer through the membrane.

#### 2. Material and methods

#### 2.1. Fluoxetine

Pharmacological fluoxetine (purity > 98%) was purchased from the local pharmaceutical market. Test solutions were prepared with Milli-Q water (electrical conductivity less than 4 mS cm<sup>-1</sup>) at the desired concentrations according to the experiments to be performed and in the pH range between 6.8 and 7.1. Fig. 1 and Table 1 show the chemical structure and characteristics of FLU.

#### 2.2. Experimental methods

- First, the hydraulic permeability of the membrane was evaluated.
- Second, we performed experiments with a fixed FLU concentration (20 mg L<sup>-1</sup>) and changed the pressure to evaluate the effect on the permeation flux and membrane rejection.
- We used a pressure of 600 kPa to validate the effect of the concentration gradient on FLU permeation through the membrane.
- We subsequently calculated the parameters of the solution–diffusion model to evaluate the reverse osmosis as a barrier to retain FLU.

#### 2.3. Reverse osmosis set-up

An apparatus for filtration (Fig. 2) was assembled using an ultra-low-pressure aromatic polyamide (PA) RO membrane with polysulfone support (ULP 2012-100, Vontron). The membrane contained a spiral wound configuration, with an area of 0.56 m<sup>2</sup> and 96% chloride rejection (measured with a solution containing 2 g L<sup>-1</sup> of NaCl at 3 bar and recovery of 15%). This configuration allows the membrane to be applied as a residential water purifying device in the hospital and laboratory from the treatment of feedwater with a concentration of solutes lower than 250 mg L<sup>-1</sup> [29].



Fig. 1. Fluoxetine structure formula. *Source*: Nebout et al. [17].

Table 1 Fluoxetine characteristics

Class	Antidepressant
<i>M</i> (g mol <sup>-1</sup> )	309.33 [27]
pK <sub>ow</sub>	4.6 [27]
pK <sub>a</sub>	9.8 [28]
Solubility at 25°C (mg L <sup>-1</sup> )	17.000 [28]
Molar volume (cm <sup>3</sup> )	266.7 [28]



Fig. 2. Pilot reverse osmosis apparatus. FT: feed tank; BV: ball valve; DP: diaphragm pump; ROM: reverse osmosis membrane; P: permeate; R: retained; PT: pressure transducer; TT: temperature transducer; GV: globe valve.

The tank volume was 4 L, and in all tests, the same volume of solution was prepared; the equipment operated between 0 and 700 kPa, and the operating conditions were adjusted so that the experiment was performed with total recovery. The permeated flux was measured using a Marte® balance model AS 2000C. The temperature was  $21^{\circ}C \pm 2^{\circ}C$ .

## 2.3.1. Effect of pressure on solvent flux and membrane rejection

Solutions with 20 mg  $L^{-1}$  of FLU were prepared in Milli-Q water and tested at the different system operating pressures (100–700 kPa). After 1 h of recirculation, the retentate and permeate samples were taken for analysis.

Membrane rejection to FLU was calculated using Eq. (1):

$$R = 1 - \frac{C_p}{C_r} \tag{1}$$

where *R* is the membrane rejection coefficient,  $C_p$  is the permeate concentration, and  $C_r$  is the tailing concentration. These data were collected to evaluate the permeation

of the water flow (solvent) through the membrane, which is necessary to evaluate the total transport of solute to permeate.

#### 2.3.2. Permeation at different concentrations

This step was performed at a constant pressure of 600 kPa. The procedure was performed at different FLU concentrations: 1.0, 5.0, 10, 15, and 20 mg L<sup>-1</sup> (in duplicate). The pressure was selected based on reports from other researchers on the removal of emerging contaminants [5,30]. After 1 h of recirculation, retentate and permeate samples were taken for analysis.

#### 2.4. Solution-diffusion model

We evaluated the solution-diffusion model to describe the passage of FLU through the RO membrane. There is an extensive description and detailed mathematical approach in the reviews of Al-Obaidi et al. [25] and Wang et al. [26]. This model involves membrane transport mechanisms in which the solvent and solute dissolve individually in the membrane surface layer and then diffuse into the matrix as separate streams through the driving force exerted by the pressure and concentration gradients. Solvent and solute fluxes are influenced by their specific diffusivity and membrane solubility coefficients [25]. It was developed by Lonsdale in 1965 and considers that the membrane surface is homogeneous and non-porous. The solvent and solute flow equations of this model are shown in Eqs. (2) and (3), respectively, where they are directly dependent on their gradients [31,32].

Eqs. (4) and (5) show the equations for the solvent and solute permeability coefficients, respectively. From these equalities, Eqs. (2) and (1) can be rewritten as shown in Eqs. (6) and (7).

$$J_w = \frac{D_w C_w V_w K_{\rm is}}{RT\Delta x} \left( \Delta P - \Delta \pi \right) \tag{2}$$

$$J_s = \left(\frac{D_s K_{js}}{\Delta x}\right) \Delta C_s \tag{3}$$

$$A = \frac{D_w C_w V_w K_{\rm is}}{RT\Delta x} \tag{4}$$

$$B = \frac{D_s K_{js}}{\Delta x}$$
(5)

$$J_w = A \left( \Delta P - \Delta \pi \right) \tag{6}$$

$$J_s = B\Delta C_s \tag{7}$$

where  $D_w$  is the diffusivity of the solvent in the membrane,  $C_w$  is the solvent concentration of the feed side,  $V_w$  is the molar volume of the feed side component,  $\Delta x$  is the thickness of the membrane,  $D_s$  is the diffusion of the solute in the membrane,  $K_{is}$  is the sorption coefficient of the solvent,

and  $K_{js}$  is the sorption coefficient of the solute. *A* and *B* represent hydraulic permeability and solute permeability, respectively.

The molar volume of water ( $V_w$ ) was calculated at different concentrations, and its mean value ( $1.65 \times 10^{-5} \text{ m}^3 \text{ mol}^{-1}$ ) was used. Sorption coefficients can be calculated from the concentrations of the components in the solution and membrane, as demonstrated by Eqs. (8) and (9).

$$K_{\rm is} = \frac{C_w(m)}{C_w} \tag{8}$$

$$K_{js} = \frac{C_p(m)}{C_R} \tag{9}$$

where  $V_w$  is the specific volume,  $C_{w(m)}$  is the concentration of solvent in the membrane,  $C_{p(m)}$  is the solute concentration in the membrane, and  $C_R$  is the solute concentration in the retentate. We calculated the Reynolds number (Re = 75.000) on the retentate side. As the turbulent flow was checked, we neglected the concentration polarization, and  $C_m$  was approximated to  $C_p$ . We considered the active layer ( $\Delta x$ ) as 1 µm, obtained from the scanning electron microscopy (SEM) images (Fig. 5).

#### 2.5. Analysis

Samples of FLU were analyzed by a high-performance liquid chromatography coupled to a mass spectrometer in the series (LC-MS/MS) in the equipment supplied by Shimadzu.

Reverse-phase chromatography with an analytical column XR-ODS III (150 × 2.0 mm × 2.0  $\mu$ m) was used, and the mobile phase used was based on Cardoso [33] consisting of mobile phase *A*: methanol and *B*: acidified water with 0.1% formic acid in the isocratic mode. The mobile phase flow rate was 0.3 mL min<sup>-1</sup>, injection volume: 10  $\mu$ L; ionization source: ESI; triple quadrupole mass analyzer operating in MS/MS mode; chromatographic analysis time:

2 min; column temperature: 40°C; capillary voltage: 4.5 kV; desolvation temperature: 400°C; desolvation gas flow rate ( $N_2$ ): 600 L h<sup>-1</sup>; spray flow: 80 L h<sup>-1</sup>; collision gas flow (argon): 0.10 mL min<sup>-1</sup>; supply temperature: 150°C.

The membrane was subjected to SEM using TESCAN (model VEGA LM 3) to determine the thickness of the top layer of the membrane. This value ( $\Delta x$ ) is required for application in the solution–diffusion model. The membrane was metalized in a Quorum Q150 R with a 10 nm Au/Pd layer. Additionally, the elementary chemical analyses of the membrane by energy-dispersive X-ray spectroscopy (EDS) supplied by the Oxford instruments model Max was performed.

#### 3. Results

The permeability of the membrane was  $3.16 \text{ L} \text{ h}^{-1} \text{ m}^{-2} \text{ bar}^{-1}$  with pure water, well within the range of permeabilities obtained by Bueno [34] in three commercial reverse osmosis (4.20, 2.80, and 1.93 L h<sup>-1</sup> m<sup>-2</sup> bar<sup>-1</sup>).

The permeate flux of the RO membrane in the separation of FLU at different pressures is shown in Fig. 3. We can observe that higher pressures promoted higher permeate flux. There was no reduction in flux over time. At 700 kPa we observed a decay of only 6% in the value of flux after 60 min of experiments. We calculated the Reynolds number to be 75.000, promoting high turbulence in the free channel for the retentate passage, and thus, it reduced the polarization concentration. In addition, after a deionized membrane wash, the pure water flow returned to nearly the initial value, indicating no deposits or clogging in the membrane.

Table 2 shows the FLU rejection by the RO membrane under different pressures. The pressure has no effect on membrane rejection, as postulated by the solution–diffusion model, where the theory proposes an uncoupling of the permeation of solvent and solute. The average rejection of FLU was 99.48% (in the range of 99.05% to 99.85%). From the point of view of applications, we can focus on the design of the treatment looking for a high rate system (higher permeation), and thus, using high pressures. However, the high



Fig. 3. Permeate flux of RO membrane in the separation of fluoxetine (20 mg L<sup>-1</sup>) at different pressures.

water flux promotes a high passage of solutes by convection to the permeate side, driving the so-called dilution effect and to an apparently better rejection. However, in the tested range, water permeation had no effect on the selectivity of the membrane.

Fig. 4 shows the dependency of the passage of FLU through the RO membrane with the concentration gradient. The determination coefficient ( $R^2 = 0.9355$ ) is large enough to conclude that the relationship between the axes is linear, as postulated by the solution–diffusion model.

From Eq. (6) and water permeability, we calculated the diffusivity of water  $(D_w)$  through the membrane as 8.75.10<sup>-7</sup> m<sup>2</sup> s<sup>-1</sup>. Similar to that, from Eq. (7) and Fig. 4, we calculated the diffusivity of FLU  $(D_s)$  as 3.48 × 10<sup>-11</sup> m<sup>2</sup> s<sup>-1</sup>. The ratio of the parameters  $(D_w/D_s)$  was 251.000.

Figs. 5 and 6 show the SEM images of the RO membrane. We considered the cross-section ( $\Delta x$ ) of the polyamide layer of approximately 1 µm to calculate the diffusivities of the solute and solvent in the solution–diffusion model. Furthermore, we found fluorine in the membrane by EDS analysis (Fig. 6). This fluorine contamination remained in the matrix of the polysulfone (PS) layer even after cleaning

Table 2

Fluoxetine rejection of the RO membrane at different pressures when  $C_0 = 20 \text{ mg L}^{-1}$ 

Pressure	Rejection (%)
100 kPa	$99.85 \pm 0.21^{a}$
200 kPa	$99.80 \pm 0.28^{a}$
300 kPa	$99.00 \pm 0.14^{a}$
400 kPa	$99.45 \pm 0.78^{a}$
500 kPa	$99.05 \pm 1.34^{a}$
600 kPa	$99.55 \pm 0.64^{a}$
700 kPa	$99.70 \pm 0.42^{a}$

aindicates statistically similar values in the same row.

in alkaline (pH 10.5) and acidic (pH 3.0) substances with NaOH and  $HNO_3$ , indicating that the dissociation of FLU salt in water releases fluorine that also permeates through the membrane. However, the fluorine was removed from the surface polyamide layer by the cleaning protocols, while the acid and alkaline cleaning routines were not able to remove it from the inner PS layer.

#### 4. Discussion

Table 2 shows that the selectivity of the membrane did not change under different fluoxetine pressures by diluting the permeate. The diluting effect of permeate Mahlangu et al. [35] or the adsorption of organic solutes on the membrane surface (it increases the concentration inside the polarized layer, and can reduce the rejection) can change the membrane rejection, as shown by Liu et al. [36]. However, the rise in pressure (Table 2) did not change the FLU rejection because the concentration of solute in the feed was too low.

The membrane rejection of FLU in our experiments (>98%) is similar to that obtained from other studies for several pharmaceuticals [3,4,19,37]. Alonso et al. [11] the high rejection of antibiotics by RO membranes was reported as in the case of 99.96% of ciprofloxacin (FLU-like structure with comparable molar mass and presence of fluoride). In addition, Hajubabania [38] RO membranes were also tested for their capability to remove FLU from water, and a rejection rate of up to 98% was found. All studies showed a small passage of pollutants through the membranes, as explained by the solution–diffusion mechanism.

The pH of the solution plays an important role in the separation of organic pollutants by NF and RO membranes because it affects the charge of the solute and the polyamide membrane. At a pH below the pKa, most of the acid functional groups are neutral and specific solute-membrane interactions prevail. The pKa of FLU is 9.8 (Table 1), and, thus, it is mostly neutral in pH in our experiments (6.8–7.0). However, polyamide membranes have surface functional



Fig. 4. Fluoxetine flux through reverse osmosis membrane at different concentration gradients.



Fig. 5. SEM image of the cross-section of the RO membrane.

groups, including carboxyl and amino groups, which are attributed to the membrane fabrication technique. Carboxyl groups can be deprotonated (thus, becoming charged), while amine groups can be protonated, and acquire a positive charge [4]. However, Wang et al. [26] reported that the dense PA layer is highly negative as acyl chloride groups are not fully converted to amide during the formation process. Strong solute-membrane interactions (including adsorption) can decrease the rejection; in some cases, this effect is appreciable even when the solute has a molar weight higher than the molar weight cut off (MWCO) of the membrane Dražević et al. [24]. The rejection of various organic compounds with different molecular weights, hydrophobicity, and charge were evaluated by Van Der Bruggen et al. [39]. They permeated the solutes in different NF membranes and found that both the membrane charge and cut off are relevant characteristics in the rejection.

The solution-diffusion model has parameters to predict the interaction between the constituents of the solution and the membrane. In the solution-diffusion theory, the separation occurs by the partitioning-diffusion mechanism in which species permeate and are dissolved in the material that composes the membrane, and then diffuses through their thickness powered by the gradient of chemical potential until the desorption step on the permeate side [4]. The ratio of  $D_{w}$  and  $D_{s}$  shows the diffusion selectivity of the membrane [40]. The ratio  $D_m/D_s$  in our work results in 251.000. For a crude comparison, MFI-type zeolites exhibit p-xylene/o-xylene selectivity over 10.000 based on differences in the isomer kinetic diameters. The diffusion coefficients of organic solutes estimated by Dražević et al. [24] were very low (between and 10<sup>-14</sup> m<sup>2</sup> s<sup>-1</sup> and 10<sup>-16</sup> m<sup>2</sup> s<sup>-1</sup>) within RO membranes. Thus, the low-pressure reverse osmosis membrane shows high selectivity for separating FLU from water.

The solution-diffusion model has been widely considered as one of the simplest non-porous or homogeneous models related to the transport mechanism through the membrane Al-Obaidi et al. [25]. Solute and solvent diffuse through the membrane independently, each using its own chemical potential Wang et al. [26]. The existence of two steps in the process of permeation of the solute through the membrane was confirmed by Ozaki and Li [41]. First, the solute is adsorbed by the membrane and it then passes through the membrane by diffusion or convection. The nature of organic compounds that influence solute adsorption includes their water solubility, acidity, and hydrogen binding capacity Dražević et al. [24]. The adsorption of different pharmaceutical pollutants on the top PA layer of RO/NF membranes was studied by Liu et al. [42]. The adsorption capacity of the membranes was mainly attributed to electrostatic attraction/repulsion and hydrophobic interactions, where the modified chemistry of the top layer with more OH<sup>-</sup> groups make the polyamide with a higher capacity form hydrogen bonds with charged PhACs. FLU is neutral at pH 6.8, and, thus, diffusion through the membrane is regarded as partitioning on the PA layer.

The difference in diffusion rates of the solute passing through the membrane is the main reason for the differences in rejection. The diffusion coefficient  $(D_s)$  establishes the kinetic property that reflects the mobility of the solute. The  $D_s$  values found in this study were low, in the order of  $3.48 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$  and, according to Dražević et al. [24], low values of  $D_s$  indicate strongly impeded solute diffusion. The permeation of the constituents is defined by the competition between size exclusion, electrical repulsion, hydrophobic interactions, and sorption/diffusion mechanisms of hydrophilic compounds, mainly related to the average pH [3,4,26]. In our experiments, water had a mobility 251.000 times higher than FLU into the matrix of the RO membrane, and thus shows a highly selective separation.

It should be noted that the main assumption of Fick's law is that the permeant species flows through a homogeneous matrix of a membrane Nagy et al. [43]. However, we estimated the effective diffusivity (instead of the real diffusivity of solute into the PA layer) because the membranes have imperfections as defects on the porous, excessive roughness, and voids in the top layer, as shown by Lin et al. [44] in the transmission electron microscopy and SEM images. The partitioning coefficient is related to the interaction of organics with both water and polyamide, and it is strongly dependent on the water content of the membrane [24]. However, the use of effective diffusivity to predict the transport of solutes and solvents in simple situations can be an advantage. For example, this simplicity of the model explains the pure diffusion of uncharged organic solutes through charged electrodialysis membranes [45].

Another aspect of the solution-diffusion model applied to polyamide membranes is the presence of the polysulfone support layer. We neglected the PS support layer, but Ramon et al. [46] claimed that support membranes with high porosity and small skin layer pores result in high water and salt permeability because the effective diffusive path length for water and salt is shorter. However, the study of Ramon et al. [46] was only theoretical using geometric simulations and the real effect of the support layer was neglected because the convective flux in the PS layer was stronger than the diffusive flux. In the framework of the resistance model, despite the higher thickness (approximately 170 µm in Fig. 6), the porosity of the PS support layer of the membrane is higher than 83% Lin et al. [44]; thus, the resistance can be neglected compared to the resistance of the selective layer. We performed the EDS analysis of the aged membrane after the experiments. The membrane had a thin active layer of aromatic PA and a PS layer as the support. Carbon, oxygen, and sulfur are mostly present as they are part of the chemical constitution of membrane materials such as polyamide and polysulfone. In addition, fluorine was also identified within the polysulfone matrix, although it was absent in the PA layer. Each contaminant can interact with the membrane's constituent layers, characterizing the polarization effect. The dissociation of the FLU salt releases fluoride (F<sup>-</sup>). The low molar mass of fluorine (18 g mol<sup>-1</sup>), associated with the high negative charge, leads to an interaction with the amino groups of the PA layer and then diffusion to the PS layer. However, the cleaning procedures release F<sup>-</sup> from the surface but are not sufficient to remove it from the bottom layer. In a study using nanofiltration, Steinle-Darling et al. [47] observed higher adsorption of FLU in the PA + PS layer compared to a commercial PS membrane, indicating a higher affinity of the compounds for the PA layer.

Another aspect to be discussed is the use of lowpressure RO membranes to separate FLU from water. Studies demonstrate the efficiency of this configuration in the removal of drugs, as shown by Ozaki and Li [41], where they observed that once the molecular mass of the organic compound exceeds 150 g mol<sup>-1</sup>, the rejection is proportional to this mass, although there are exceptions (for example, due to dissociation of the solute). Urtiaga et al. [37] tested a low-pressure (11 bar) pilot RO system that rejected 99% of drugs such as ibuprofen, caffeine, atenolol, and hydrochlorothiazides. In his study, Mamo et al. [3] operated a lowpressure membrane system (6.5 bar) to remove pollutants such as acetaminophen, diclofenac, diazepam, and FLU, with rejection rates of approximately 99%. It is evident that the aforementioned drugs are similar to FLU in terms of chemical structure (presence of functional groups, such as amines, amides, and aromatic rings), masses, and electrostatic as well as satisfactory removal in low-pressure RO modules.

#### 5. Conclusion

Reverse osmosis is a promising technology for the removal of new pollutants from water, including fluoxetine. The ultra-low-pressure RO membrane showed high rates of FLU removal under the experimental conditions,



Fig. 6. EDS analysis of the polysulfone layer.

contributing to advanced water treatment, operating at reduced pressures, ensuring low energy consumption, and lower post-treatment expenses.

The solution-diffusion model has shown that the RO membrane is an efficient and satisfactory physical barrier for FLU. However, it must be noted that RO is not a perfect barrier, and traces of pollutants do pass through the membrane.

#### Symbols

R	—	Membrane rejection coefficient
$C_n$	_	Permeate concentration
$C_r^r$	_	Tailing concentration
$\dot{D_{w}}$	_	Diffusivity of the solvent in the membrane
$C_{w}$	_	Solvent concentration of the feed side
$V_{w}$	_	Molar volume of the feed side component
$\Delta x$	—	Thickness of the membrane
D	—	Diffusion of the solute in the membrane
$K_{is}$	—	Sorption coefficient of the solvent
$K_{is}$	—	Sorption coefficient of the solute
$A^{\beta}$	_	Hydraulic permeability
В	_	Solute permeability
$C_{w(m)}$	—	Concentration of solvent in the membrane
$C_{n(m)}$	—	Solute concentration in the membrane
$J_w$	—	Solvent flow
J	_	Solute flow
-		

#### References

- [1] R. Bade, N.I. Rousis, L. Bijlsma, E. Gracia-Lor, S. Castiglioni, J.V. Sancho, F. Hernandez, Screening of pharmaceuticals and illicit drugs in wastewater and surface waters of Spain and Italy by high resolution mass spectrometry using UHPLC-QTOF MS and LC-LTQ-Orbitrap MS, Anal. Bioanal. Chem., 407 (2015) 8979–8988.
- [2] O. Rozas, C. Vidal, C. Baeza, W.F. Jardim, A. Rossner, H.D. Mansilla, Organic micropollutants (OMPs) in natural waters: oxidation by UV/H<sub>2</sub>O<sub>2</sub> treatment and toxicity assessment, Water Res., 98 (2016) 109–118.
- [3] J. Mamo, M.J. García-Galán, M. Stefani, S. Rodríguez-Mozaz, D. Barceló, H. Monclús, I. Rodriguez-Roda, J. Comas, Fate of pharmaceuticals and their transformation products in integrated membrane systems for wastewater reclamation, Chem. Eng. J., 331 (2018) 450–461.
- [4] K.P.M. Licona, L.R. de O. Geaquinto, J.V. Nicolini, N.G. Figueiredo, S.C. Chiapetta, A.C. Habert, L. Yokoyama, Assessing potential of nanofiltration and reverse osmosis for removal of toxic pharmaceuticals from water, J. Water Process Eng., 25 (2018) 195–204.
- [5] J. Garcia-Ivars, L. Martella, M. Massella, C. Carbonell-Alcaina, M.-I. Alcaina-Miranda, M.-I. Iborra-Clar, Nanofiltration as tertiary treatment method for removing trace pharmaceutically active compounds in wastewater from wastewater treatment plants, Water Res., 125 (2017) 360–373.
- [6] S. Sulaiman, M. Khamis, S. Nir, L. Scrano, S.A. Bufo, R. Karaman, Diazepam stability in wastewater and removal by advanced membrane technology, activated carbon, and micelle–clay complex, Desal. Water Treat., 57 (2014) 3098–3106.
- [7] S.O. Ganiyu, E.D. van Hullebusch, M. Cretin, G. Esposito, M.A. Oturan, Coupling of membrane filtration and advanced oxidation processes for removal of pharmaceutical residues: a critical review, Sep. Purif. Technol., 156 (2015) 891–914.
- [8] N.H. Torres, J.H.P. Américo, L.F.R. Ferreira, C. Nazato, L.A. Maranho, F.Z. Vilca, V.L. Tornisielo, Fármacos no ambiente – revisão, Revista de estudos ambientais, 4 (2012) 67–75.

- [9] R.F. Silva, G.L. Silva, P.T.S. Silva, V.L. Silva, Identificação e Quantificação de Contaminantes Emergentes em Estações de Tratamento de Esgoto, Rev. Virtual Quim., 3 (2016) 702–715.
- [10] Y.-Y. Zhao, X.-M. Wang, H.-W. Yang, Y.-F. Xie, Effects of organic fouling and cleaning on the retention of pharmaceutically active compounds by ceramic nanofiltration membranes, J. Membr. Sci., 563 (2018) 734–742.
- [11] J.J.S. Alonso, N. El Kori, N. Melián-Martel, B. Del Río-Gamero, Removal of ciprofloxacin from seawater by reverse osmosis, J. Environ. Manage., 217 (2018) 337–345.
- [12] L.J.G. Silva, C.M. Lino, L.M.M. Meisel, A. Pena, Selective serotonin re-uptake inhibitors (SSRIs) in the aquatic environment: an ecopharmacovigilance approach, Sci. Total Environ., 437 (2012) 185–195.
- [13] A.L. Carvalho, M.R. Costa, H. Fagundes, Uso racional de psicofármacos, CPSM/SMS-Rio, 1 (2006).
- [14] J.B. Fursdon, J.M. Martin, M.G. Bertram, T.K. Lehtonen, B.B.M. Wong, The pharmaceutical pollutant fluoxetine alters reproductive behaviour in a fish independent of predation risk, Sci. Total Environ., 650 (2019) 642–652.
- [15] GERMED Farmacêutica LTDA, Cloridrato de fluoxetina. Bula. Medicamento genérico, Hortolândia/SP.
- [16] M.T. Cruz, E.L. Cruz, J.R.P. Torres, Avaliação do uso de medicamentos psicotrópicos pelos pacientes da farmácia municipal de Terra Roxa D'Oeste/PR, Revista Thêma et Scientia, 1 (2015) 131–137.
- [17] P. Nebout, B. Cagnon, S. Delpeux, A. Di Giusto, O. Chedeville, Comparison of the efficiency of adsorption, ozonation, and ozone/activated carbon coupling for the removal of pharmaceuticals from water, J. Environ. Eng., 142 (2016) 04015074: 1–6.
- [18] G. Jaria, V. Calisto, M.V. Gil, M. Otero, V.I. Esteves, Removal of fluoxetine from water by adsorbent materials produced from paper mill sludge, J. Colloid Interface Sci., 448 (2015) 32–40.
- [19] S. Rodriguez-Mozaz, M. Ricart, M. Köck-Schulmeyer, H. Guasch, C. Bonnineau, L. Proia, M.L. Alda, S. Sabater, D. Barceló, Pharmaceuticals and pesticides in reclaimed water: efficiency assessment of a microfiltration–reverse osmosis (MF–RO) pilot plant, J. Hazard. Mater., 282 (2015) 165–173.
- [20] F. Martínez, M.J. López-Muñoz, J. Aguado, J.A. Melero, J. Arsuaga, A. Sotto, R. Molina, Y. Segura, M.I. Pariente, A. Revilla, L. Cerro, G. Carenas, Coupling membrane separation and photocatalytic oxidation processes for the degradation of pharmaceutical pollutants, Water Res., 47 (2013) 5647–5658.
- [21] C.F. Couto, L.C. Lange, M.C.S. Amaral, A critical review on membrane separation processes applied to remove pharmaceutically active compounds from water and wastewater, J. Water Process Eng., 26 (2018) 156–175.
- [22] F.-C. Yen, S.-J. You, T.-C. Chang, Performance of electrodialysis reversal and reverse osmosis for reclaiming wastewater from high-tech industrial parks in Taiwan: a pilot-scale study, J. Environ. Manage., 187 (2017) 393–400.
- [23] X. Zheng, Z.X. Zhang, D.W. Yu, X.F. Chen, R. Cheng, S. Min, J.Q. Wang, Q.C. Xiao, J.H. Wang, Overview of membrane technology applications for industrial wastewater treatment in China to increase water supply, Resour. Conserv. Recycl., 105 (2015) 1–10.
- [24] E. Dražević, K. Košutić, M. Svalina, J. Catalano, Permeability of uncharged organic molecules in reverse osmosis desalination membranes, Water Res., 116 (2017) 13–22.
- [25] M.A. Al-Obaidi, C. Kara-Zaitri, I.M. Mujtaba, Scope and limitations of the irreversible thermodynamics and the solution–diffusion models for the separation of binary and multi-component systems in reverse osmosis process, Comput. Chem. Eng., 100 (2017) 48–79.
- [26] J.W. Wang, D.S. Dlamini, A.K. Mishra, M.T.M. Pendergast, M.C.Y. Wong, B.B. Mamba, V. Freger, A.R.D. Verliefde, E.M.V. Hoek, A critical review of transport through osmotic membranes, J. Membr. Sci., 454 (2014) 516–537.
- [27] B.W. Brooks, C.M. Foran, S.M. Richards, J. Weston, P.K. Turner, J.K. Stanley, K.R. Solomon, M. Slattery, T.W. La Point, Aquatic ecotoxicology of fluoxetine, Toxicol. Lett., 142 (2003) 169–183.

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- [28] Human Metabolome Database (HMDB), Disponível em: http:// www.hmdb.ca/metabolites/HMDB0014615.
- [29] VONTRON TECHNOLOGY Co. Ltd., Manual of Product, Technical Support and Service, 148 p.
- [30] V. Yangali-Quintanilla, S.K. Maeng, T. Fujioka, M. Kennedy, Z.Y. Li, G. Amy, Nanofiltration vs. reverse osmosis for the removal of emerging organic contaminants in water reuse, Desal. Water Treat., 34 (2011) 50–56.
- [31] F. Macedônio, E Drioli, Fundamentals in Reverse Osmosis, Comprehensive Membrane Science and Engineering, 2nd ed., 2017, pp. 79–94.
- [32] R.W. Baker, Membrane Technology and Applications, 2nd ed., Wiley Publisher, 2004.
- [33] L.V. Cardoso, Otimização e validação de método empregando SPE E LC-APCI-MS/MS para determinação de fármacos em água de superfície e de abastecimento público (2011), Dissertação (Mestrado em Química) - Universidade Federal do Rio Grande, 2011.
- [34] M.Z. Bueno, Nanofiltração e osmose inversa aplicadas à remoção de agrotóxicos (carbamatos) em águas de abastecimento: avaliação em escala de bancada (2013), 194, Dissertação (Mestrado em Engenharia Ambiental) - Universidade Federal de Santa Catarina, Florianópolis, 2013.
- [35] T.O. Mahlangu, E.M.V. Hoek, B.B. Mamba, A.R.D. Verliefde, Influence of organic, colloidal and combined fouling on NF rejection of NaCl and carbamazepine: role of solute-foulantmembrane interactions and cake-enhanced concentration polarization, J. Membr. Sci., 471 (2014) 35–46.
  [36] Y.-L. Liu, X.-M. Wang, H.-W. Yang, Y.-F. Xie, Adsorption of
- [36] Y.-L. Liu, X.-M. Wang, H.-W. Yang, Y.-F. Xie, Adsorption of pharmaceuticals onto isolated polyamide active layer of NF/ RO membranes, Chemosphere, 200 (2018) 36–47.
- [37] A.M. Urtiaga, G. Pérez, R. Ibáñez, I. Ortiz, Removal of pharmaceuticals from a WWTP secondary effluent by ultrafiltration/reverse osmosis followed by electrochemical oxidation of the RO concentrate, Desalination, 331 (2013) 26–34.
- [38] S. Hajubabania, Effect of Fouling on Removal of Trace Organic Compounds by Nanofiltration, Tese, (Mestrado em Engenharia de Pesquisa), School of Chemical Engineering University of New South Wales, Sydney, Australia, 2010, 173 p.

- [39] B. Van Der Bruggen, A. Verliefde, L. Braeken, E.R. Cornelissen, K.M. Jasper, Q.J.C. Verberk, H.J.C. van Dijk, G. Amy, Assessment of a semi-quantitative method for estimation of the rejection of organic compounds in aqueous solution in nanofiltration, J. Chem. Technol. Biotechnol., 81 (2006) 1166–1176.
- [40] Y. Ma, F.Y. Zhang, S.W. Yang, R.P. Lively, Evidence for entropic diffusion selection of xylene isomers in carbon molecular sieve membranes, J. Membr. Sci., 564 (2018) 404–414.
  [41] H. Ozaki, H.F. Li, Rejection of organic compounds by
- [41] H. Ozaki, H.F. Li, Rejection of organic compounds by ultra-low pressure reverse osmosis membrane, Water Res., 36 (2002) 123–130.
- [42] Y.-L. Liu, X.-M. Wang, H.-W. Yang, Y.-F. Xie, Quantifying the influence of solute-membrane interactions on adsorption and rejection of pharmaceuticals by NF/RO membranes, J. Membr. Sci., 551 (2018) 37–46.
- [43] E. Nagy, M. Meiczinger, M. Vitai, Investigation of the improvement of energy generation by pressure retarded osmosis, J. Membr. Sci. Res., 5 (2019) 137–146.
- [44] T. Lin, S.L. Yu, W. Chen, Occurrence, removal and risk assessment of pharmaceutical and personal care products (PPCPs) in an advanced drinking water treatment plant (ADWTP) around Taihu Lake in China, Chemosphere, 152 (2016) 1–9.
- [45] L.S. Ma, L. Gutierrez, M. Vanoppen, D.N. Lorenz, C. Aubry, A. Verliefde, Transport of uncharged organics in ion-exchange membranes: experimental validation of the solution–diffusion model, J. Membr. Sci., 564 (2018) 773–781.
- [46] G.Z. Ramon, M.C.Y. Wong, E.M.V. Hoek, Transport through composite membrane, part 1: is there an optimal support membrane?, J. Membr. Sci., 415–416 (2012) 298–305.
- [47] E. Steinle-Darling, E. Litwiller, M. Reinhard, Effects of sorption on the rejection of trace organic contaminants during nanofiltration, Environ. Sci. Technol., 44 (2010) 2592–2598.
- [48] M. Taheran, S.K. Brar, M. Verma, R.Y. Surampalli, T.C. Zhang, J.R. Valero, Membrane processes for removal of pharmaceutically active compounds (PhACs) from water and wastewaters, Sci. Total Environ., 547 (2016) 60–77.