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REMOVAL OF DRUGS FROM AQUEOUS MATRIXES USING A REVERSE OSMOSIS MEMBRANE

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Abstract: Pollution of water bodies by micropollutants is a problem of growing concern, especially regarding contamination with drug residues and metabolites. The presence of these substances in surface waters is related to deleterious consequences for the population and the environment. The incorrect disposal of drug residues and the low efficiency of conventional water treatment methods require the use of alternative methods, such as the use of membrane separation processes for the treatment of effluents. The present study aimed to evaluate the efficiency of a reverse osmosis membrane for the removal of ibuprofen and diclofenac sodium from an aqueous matrix. For this, permeation tests were performed with aqueous solutions of diclofenac and ibuprofen at a concentration of 10 $mg \cdot L^{-1}$, alone and together. The hydraulic permeability of the membrane and the drug rejection efficiency were evaluated. The presence of drugs in the solution had little influence on the hydraulic permeability of the membrane. The minimum removal efficiency of both substances was greater than 98.5 %, generating a permeate stream practically free of drugs, whether evaluated separately or in the same solution. These results indicate the operational robustness of the membrane since neither the permeability nor the rejection were altered by the fact that we have the two drugs combined, in addition to demonstrating the potential use of reverse osmosis as a treatment method for the removal of residues and traces of drugs and other difficult-to-treat organic substances in aqueous matrices.

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INTRODUCTION

Population growth causes the demand for water resources to grow exponentially. The Brazilian National Water Agency (2022) estimates that of the 2.5 % of freshwater present in the world, 69.0 % is difficult to access, and only 1.0 % is found in rivers. Even more important than quantity is the quality of water for human consumption. Due to its properties as a solvent, this fluid is associated with several impurities incorporated in it, such as, for example, drug residues.

The significant increase in drug consumption is due, in addition to population growth, to the expiration of patents and the production of generics with lower market prices. In addition, the bad habit of self-medication ends up generating an accumulation of medicines in homes, which conditions the expiration and improper disposal of these substances (TANNUS, 2017; FOREAUX et al., 2019).

Even at concentrations as low as micro and nanograms per liter, because they are difficult to degrade biologically, drugs are considered "emerging pollutants". These are thus known to be compounds with increasing consumption, already detected in effluents and water bodies, and cause important environmental impacts. In addition, they are on the list of government concerns, which makes them a focus for possible restrictions in legislation (PIRETE, 2018).

The presence of drugs in surface water, even in extremely low concentrations, is of great concern from an environmental point of view. The consumption of these substances in water can cause several endocrine and reproductive disorders and congenital problems in animals. The direct effects caused on the endocrine system are of most concern because even at low concentrations, these drug residues can cause various health problems, such as reduced fertility, cancers in the reproductive system, and congenital alterations (LIMA et al., 2017).

Improper disposal of antibiotics in the environment can also cause toxicity effects and the development of antibiotic resistance in bacteria. It is important to note that many drugs have a hormonal effect on living beings (xenoestrogens or endocrine disruptors), which can cause biological changes, such as the feminization of male fish (TAMBOSI, 2008).

Bila and Dezotti (2003) commented on the induction of male fish of the species *Oryzias latipes* to hermaphroditism in the presence of residues of estrogenic substances in effluents from an effluent treatment plant at concentrations ranging from 30 to 500 $ng \cdot L^{-1}$. Exposure of male fish to effluents for 150 days induced feminization of fish. Back in natural (unpolluted) waters, no new sexual changes occurred in the fish, demonstrating that the changes in the reproductive system were permanent.

Stanford et al. (2010) evaluated the potential for hormonal alteration (estrogenicity) of mineral water relative to 40 other food products. All items showed estrogenic effects, except for drinking water and one type of apple juice. The researchers reported that the risk of endocrine system alterations from food consumption would be between 4 and 21 times greater than from consumption of drinking water.

Brazilian studies have tracked drug concentrations higher than those found in international studies, which are directly proportional to population density and dry periods in the studied locations. Ghiselli and Jardim (2007) believe that the explanation lies in the lack of sanitary structure found in the Brazilian scenario. Lima et al. (2017) compiled data on microcontaminants present in natural and treated waters in Brazil, reporting the presence of drug residues such as acetylsalicylic acid, amoxicillin, diclofenac, and ibuprofen, with concentrations in the range of nanograms and micrograms per liter in both treated and raw water.

The incorrect disposal of expired or deteriorated medicines, in landfills or even in sinks and toilets, leading to the worsening of this scenario. In addition, the human body is not capable of completely metabolizing many of the drugs ingested, which are excreted in the form of feces or urine in the public sewer system. Often, the products of drug metabolism themselves can have a hormonal effect, which further aggravates the situation. Since these drug residues or their metabolites are not treated efficiently while in the effluents, they are released into water bodies, enhancing the harmful effects on the environment (XIANG et al., 2019).

This is because conventional effluent treatment stations have steps aimed at removing particulate matter and microorganisms, in addition to controlling physical-chemical parameters. However, because drugs are biochemically active compounds in aquatic environments, traditional treatments are ineffective regarding their removal from effluents (LIMA et al., 2017).

As the conventional treatment of effluents is not efficient in the removal of drugs, it becomes necessary to look for alternative solutions for the decontamination of these waters. Among the different proposed methods, there is the use of membrane separation processes as a possible form of treatment for the removal of these difficult-to-remove molecules (XIANG et al., 2019; HOLLMAN et al., 2020).

Among the complementary treatment techniques that are effective in removing particles smaller than one micrometer, the use of nanofiltration and reverse osmosis (RO) membranes stands out. Despite the higher cost compared to other methods, these processes are highly efficient in terms of removing microcontaminants (LIMA et al., 2017; XIANG et al., 2019; HOLLMAN et al., 2020).

Widely used for the separation of compounds with low molar mass (such as ions and molecules below 500 Da), RO membranes are used in the treatment of drinking water from effluents, with the potential to remove dissolved microcontaminants such as pesticides and drugs (HOWE et al., 2016).

According to Pirete (2018), between the years 2000 and 2017, about a quarter of the studies carried out with membranes for drug removal (such as diclofenac and caffeine) used reverse osmosis membranes. Bueno et al. (2016) evaluated the removal of carbofuran, the active ingredient of some pesticides, in three aqueous matrices: ultrapure, raw, and pre-treated water. At a pressure of 30 bar, 99.7 % of the substance was removed with a transmembrane flow of 49.7 $L{\cdot}m^{-2}{\cdot}h^{-1}$.

Licona et al. (2018) evaluated the use of reverse osmosis in the treatment of aqueous synthetic solutions with the drugs ibuprofen, paracetamol, diclofenac, dipyrone, and caffeine. The removal efficiency of ibuprofen, diclofenac, and dipyrone was 98 %.

In general, high removal rates are found, but the greatest difficulty is in understanding the contribution of each compound alone since they are present in a combined form in a single aqueous matrix (LICONA et al., 2018). Membrane separation processes, as they encompass several mechanisms to remove micropollutants (such as size exclusion, electrostatic repulsion, hydrophobic interaction, or adsorption), are influenced by the presence of different constituents of the aqueous matrix (LIN; CHIOU; LEE, 2017; XIANG et al., 2019; HOLLMAN et al., 2020).

The water-solute interaction, the material used in the membrane, and the operating conditions (temperature, pressure, flow, feed rate) are also factors that influence the efficiency of the process. It is necessary to establish/determine the optimal operating conditions for membranes and reverse osmosis systems at an industrial level, so that high rates of contaminant removal can be obtained with high productivity and cost reduction (LICONA et al., 2018; HOLLMAN et al., 2020).

In this scenario, the present work aimed to evaluate the efficiency of the use of reverse osmosis in the removal of the drugs diclofenac sodium and ibuprofen, aiming to evaluate the impact of the presence of the two drugs combined on the performance of a commercial membrane.

DEVELOPMENT

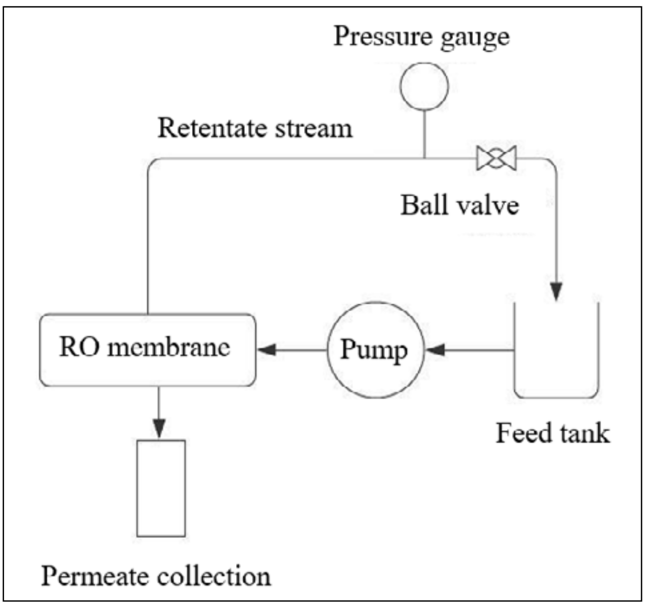
MATERIALS AND METHODS

The drugs used, sodium diclofenac (DCF) and ibuprofen (IBU), were supplied by Sigma-Aldrich (USA). The reverse osmosis membrane used was a spiral wounded module made of polysulfone, manufacturer Metagoal®, model TFC-2002-100G, with a useful permeation area of 3,500 cm², 20 cm in length, and a molecular weight cut-off (MWCO) of approx. 100 Da.

Three feeding solutions were prepared, one containing DCF, another containing IBU, and a third containing both drugs. Drug concentrations of 10 $mg \cdot L^{-1}$ were used in all feed solutions, prepared in distilled water. The pH of the feed solution containing IBU was approx. 4.5. the feed containing DCF had a pH of approx. 5.7, and the feed solution containing both drugs had a pH of approx. 5.0.

To carry out the permeation tests, a reverse osmosis module was used, whose simplified scheme is shown in Figure 1.

Figure 1 - Diagram of the reverse osmosis system used in the permeation tests.



Source: Authors (2023).

The permeate flux was calculated according to Equation (1):

$$J_P = \frac{V}{A \times t} \quad (1)$$

Being ‘ J_p ’ the permeate flux ($L \cdot m^{-2} \cdot h^{-1}$), ‘$V$’ the volume of permeate (L) collected in the time ‘t’, ‘A’ the useful membrane permeation area (m^2), and ‘t’ is the permeate collection time interval (h). To calculate the hydraulic permeability in each test, Equation (2) was used:

$$L_P = \frac{J_P}{\Delta P} \tag{2}$$

Where ‘ L_p ’ is the hydraulic permeability of the membrane ($L \cdot m^{-2} \cdot h^{-1} \cdot bar^{-1}$) and ‘ ΔP ’ is the transmembrane pressure (bar). The drug retention efficiency was determined from Equation (3):

$$R = \frac{C_A - C_P}{C_A} \times 100 \tag{3}$$

Where ‘R ’ is the percentage retention of the analyte (%), ‘C_A ’ is the concentration of drugs in the feed stream ($mg \cdot L^{-1}$), and ‘C_P ’ is the concentration of drugs in the permeate stream ($mg \cdot L^{-1}$).

Each experiment corresponded to the steps of membrane compaction, in which the system was maintained at a constant pressure of 6 bar until the permeate flow remained stabilized for 1 h. The hydraulic permeability of the membrane was then determined using distilled water (without the presence of drugs). The permeate flux was evaluated with the transmembrane pressure variation from zero to 6 bar in 1 bar increments, with a collection interval of 10 min after the pressure change. Finally, the hydraulic permeability tests were carried out using the feed solutions containing the drugs, following the same procedure used for the tests with distilled water.

The determination of the drug rejection efficiency was performed by quantifying the drug concentration in the samples obtained from the feed and permeate streams. The quantification of drugs was performed by absorption spectroscopy in the ultraviolet-visible region. A quartz cuvette with a 1 cm optical path and a Beckman spectrophotometer, model DU530, were used. Calibration curves were produced with a concentration range from 0.3 to 100.0 $mg \cdot L^{-1}$, with a wavelength of 278 nm for the determination of sodium diclofenac and 222 nm for ibuprofen, as well as the quantification of permeate and feed streams. The limits of quantification (LQ) were 0.15 $mg \cdot L^{-1}$ for DCF and 0.05 $mg \cdot L^{-1}$ for IBU.

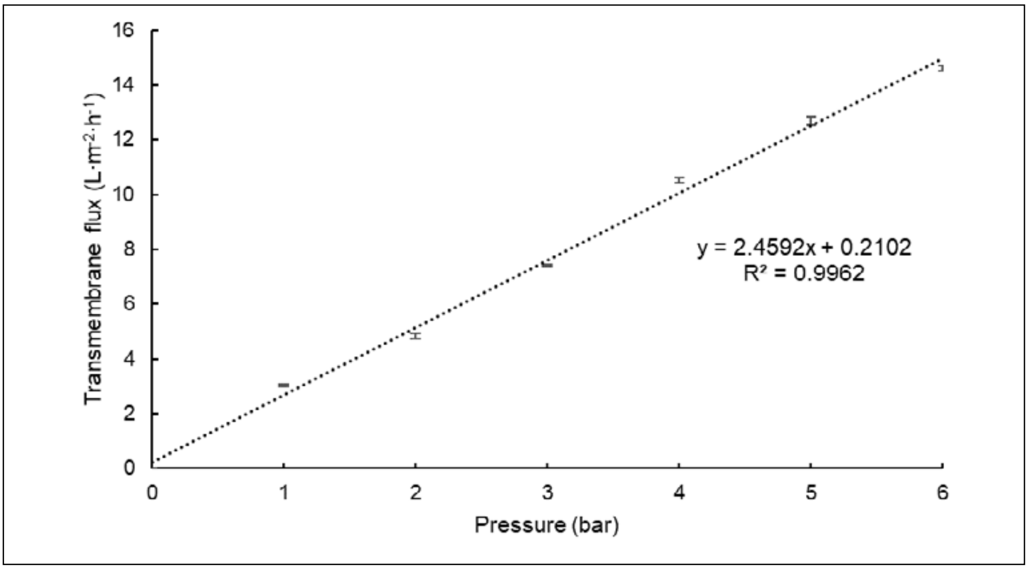
The experiment followed a completely randomized design, with three replicates for each treatment. Transmembrane flux as a function of pressure, hydraulic permeability, and drug rejection efficiency were evaluated. The data obtained were submitted to Analysis of Variance (ANOVA) and the means were compared by Tukey’s test at a 5 % probability of error. Statistical analyzes were performed using the Statistica 12 program (StatSoft, USA).

RESULTS AND DISCUSSION

Hydraulic permeability

After the membrane conditioning and compaction process, its hydraulic permeability was determined using distilled water as feed. The results obtained demonstrate that the transmembrane flow behaved proportionally and linearly to the increase in transmembrane pressure, as shown in Figure 2.

Figure 2 – Transmembrane flow as a function of applied pressure for a feed composed of distilled water.

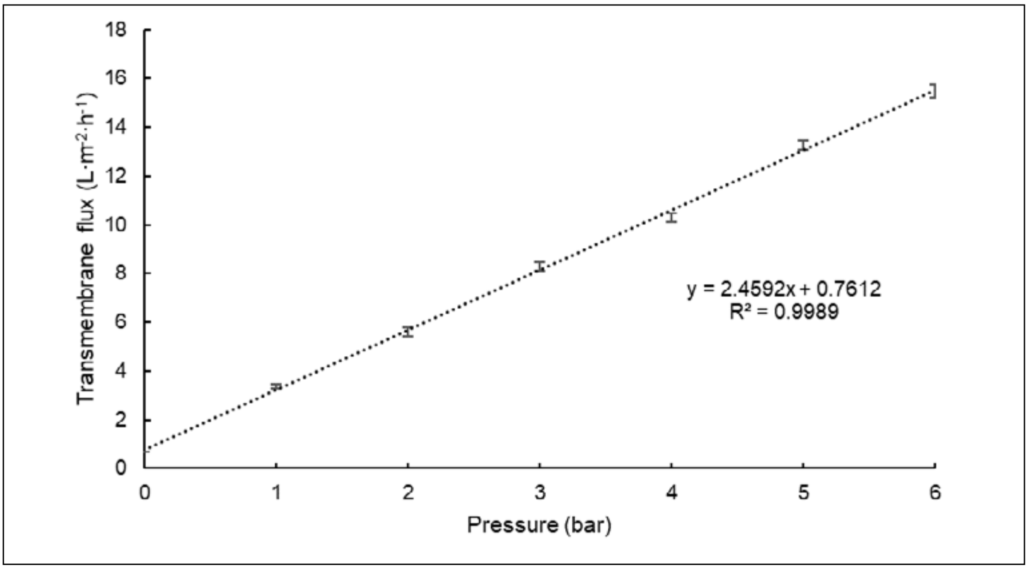


Source: Authors (2023).

According to the transmembrane flow data as a function of pressure, the estimated hydraulic permeability of the membrane was 2.46 $L \cdot m^{-2} \cdot h^{-1} \cdot bar^{-1}$. This directly proportional relationship between flow and pressure is expected for reverse osmosis membranes, considering that the main driving force in this type of separation is the chemical potential difference caused by the pressure differential between the sides of the membrane (HEO et al., 2013; XIANG et al., 2019).

Subsequently, the hydraulic permeability of the membrane in the permeation of solutions containing the drugs IBU and DCF, isolated and mixed, was determined. The transmembrane flow for the 10 $mg \cdot L^{-1}$ IBU solution relative to the pressure applied to the system is shown in Figure 3.

Figure 3 – Behavior of the transmembrane flow as a function of the pressure applied in the permeation of a feeding solution containing 10 mg·L $^{-1}$ of IBU.



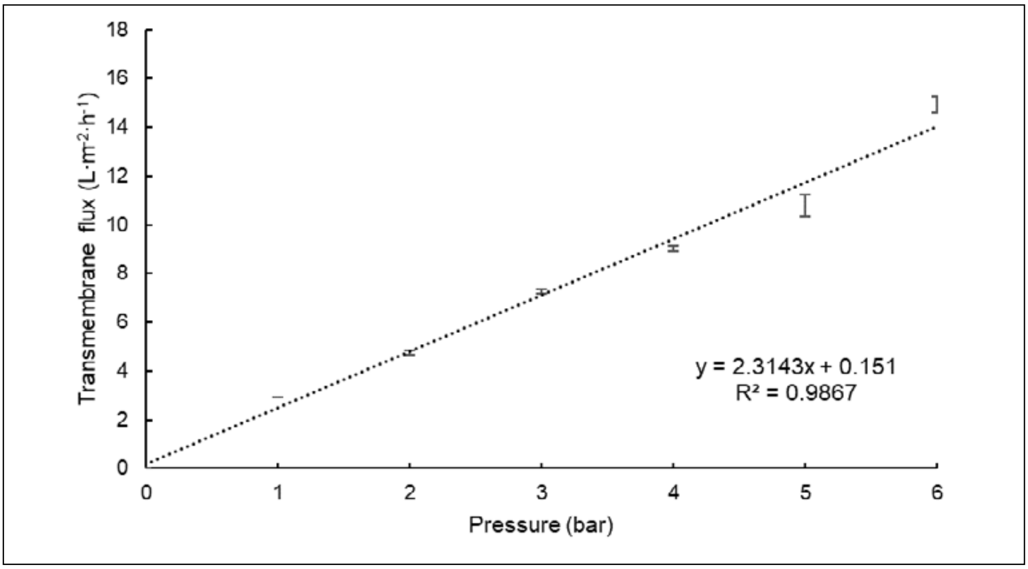
Source: Authors (2023).

A directly proportional relationship between permeate flux and pressure was observed for the solution containing ibuprofen as feed. The hydraulic permeability of the membrane concerning the ibuprofen solution was calculated to be 2.46 L·m^{-2} ·h^{-1} ·bar^{-1}. Since the fluxes found are like those of permeability in water, it is understood that the ibuprofen molecule does not have negative effects on the sorption and diffusion capacity of the membrane, fouling, or decrease in flux.

Lin, Chiou, and Lee (2014) commented that the fouling effect is a product of the presence of other materials in the feed stream, such as organic matter since the concentrations of micropollutants are too low to cause interaction effects with the membrane capable of significantly altering both flow and selectivity. In this sense, it is important that the feed goes through pre-treatment stages that guarantee the maximum removal of particulate matter and organic matter. These pre-treatment steps provide better functioning of the reverse osmosis system, reducing the need for maintenance and maintaining the efficiency of removing micropollutants, with adequate transmembrane fluxes (URITAGA et al., 2013; LIN; CHIOU; LEE, 2014).

The transmembrane flow for the DCF 10 mg·L^{-1} solution relative to the pressure applied to the system is shown in Figure 4.

Figure 4 – Behavior of the transmembrane flow as a function of the pressure applied in the permeation of a feeding solution containing 10 mg·L^{-1} of DCF.

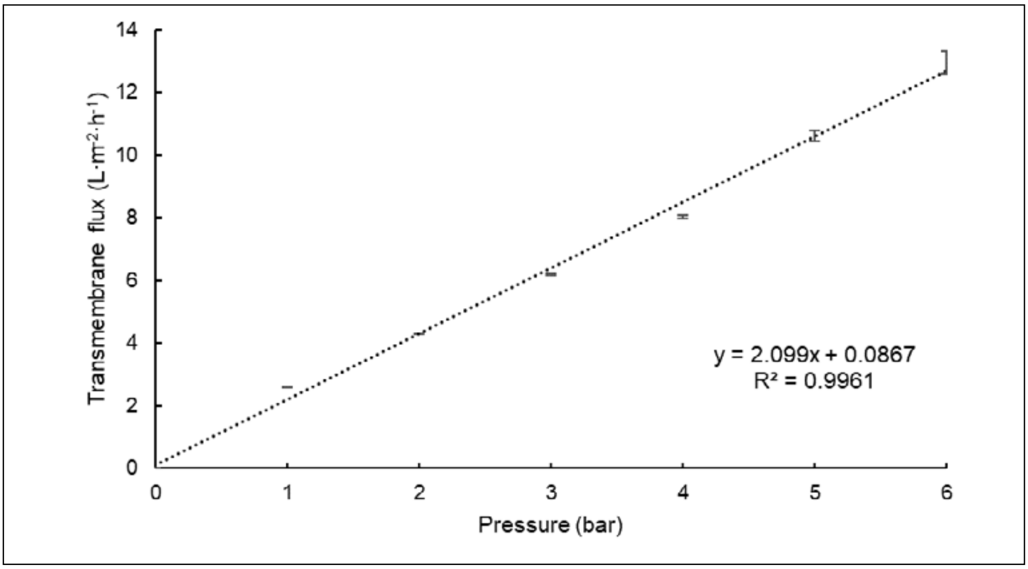


Source: Authors (2023).

The hydraulic permeability of the membrane concerning the sodium diclofenac solution was calculated as 2.31 L·m^{-2} ·h^{-1} ·bar^{-1}. RO membranes are more likely to decrease flux compared to the others since their pores are very small and have high removal efficiency rates, which can generate concentration polarization on the membrane surface with increasing pressure (FOUREAUX et al., 2019). However, the presence of sodium diclofenac did not cause an important change in the hydraulic permeability of the membrane relative to the permeation of distilled water. This is due to the low concentration of the drug, with no boundary layer effects, such as concentration polarization, which decrease the rates of sorption and diffusion of feed components through the membrane (XIANG et al., 2019; HOLLMAN et al., 2020).

The behavior of the transmembrane flux found in the permeation of the feeding solution containing both drugs at a concentration of 10 mg·L^{-1} each is shown in Figure 5.

Figure 5 - Transmembrane flow as a function of permeation pressure of a feeding solution containing IBU and DCF at a concentration of 10 mg·L^{-1} each.



Source: Authors (2023).

Thus, the hydraulic permeability of the membrane in relation to the solution containing both drugs was calculated as 2.10 L·m^{-2}·h^{-1}·bar^{-1}. There was a reduction in the hydraulic permeability of the membrane in the presence of both drugs (total concentration of 20 mg·L$^{-1,}$ 10 mg·L^{-1} DCF + 10 mg·L^{-1} IBU), but the behavior of the flow as a function of pressure maintained a linear behavior. As noted by Gholami et al. (2012), the presence of higher concentrations of solutes in the feed causes an increase in osmotic pressure and changes in the viscosity of the solution, whose interaction with the membrane can reduce, albeit to a small degree, the transmembrane flow. Dolar et al. (2011), on the other hand, comment that the adsorption of ions from the feed solution in the pores of the membrane can change its electrical balance, causing repulsion effects between chemical species with the same charge. Considering that many drugs appear ionized or as zwitterions even at neutral pH, the presence of ionized species can act as an obstacle to the membrane sorption process, delaying diffusion and decreasing transmembrane flux (LIN; CHOU; LEE, 2014; LIN, 2017; DOLAR et al., 2017).

The transmembrane flow results at 6 bar and the hydraulic permeability of the membrane in the permeation of the three feed solutions are compiled in Table 1.

Table 1 – Transmembrane flow at the highest system pressure (6 bar) and hydraulic permeability of the membrane as a function of the type of supply.

Feed	Transmembrane flow at 6 bar ($L \cdot m^{-2} \cdot h^{-1}$)	Hydraulic permeability ($L \cdot m^{-2} \cdot h^{-1} \cdot bar^{-1}$)
Distilled water	14.63±0.10 b	2.46±0.03 a
DCF 10 $mg \cdot L^{-1}$	15.49±0.26 a	2.46±0.04 a
IBU 10 $mg \cdot L^{-1}$	14.91±0.34 b	2.31±0.06 b
DCF 10 $mg \cdot L^{-1}$ + IBU 10 $mg \cdot L^{-1}$	12.97±0.36 c	2.10 ±0.04 c

Column means followed by the same letter do not differ statistically by Tukey's test at a 5 % probability of error. Source: Authors (2023).

There was a decrease in the transmembrane flow at a pressure of 6 bar, considering the feed containing both drugs. Similar behavior was observed for the hydraulic permeability of the membrane, which was lower in the permeation of the feed solution containing ibuprofen and even lower in the solution containing the two drugs concomitantly.

This behavior of reducing the transmembrane flux and permeability can be explained by the effects of interaction between the drugs or by the formation of organic fouling, which occurs when there is an accumulation of organic compounds on the surface of the membrane since both are present in the feed solution. Drugs (BORSI et al., 2012). This effect can be mainly a result of the interaction between the IBU and the membrane, as can be seen by the lower permeability of the membrane in both solutions containing this substance. Bourassi et al. (2021), evaluating the sorption potential of different hybrid membranes containing graphene, graphene derivatives, and zeolites, reported that ibuprofen was adsorbed to a greater degree on polydimethylsiloxane (PDMS) membranes, indicating a greater affinity of this drug with the polymeric matrix. Thus, ibuprofen can interact with the membrane surface more strongly, impairing the permeation of other food components, such as water.

Zelinski et al. (2023) used this same type of commercial membrane for treating effluents and obtained hydraulic permeability ranging from 4.9 – 5.6 $L \cdot m^{-2} \cdot h^{-2} \cdot bar^{-1}$ for distilled water. However, when filtering effluent from galvanic baths, permeability dropped to 0.39 – 1.49 $L \cdot m^{-2} \cdot h^{-2} \cdot bar^{-1}$, attributing the reduction in permeability to fouling effects caused by the presence of organic compounds in the feed and the interaction between the membranes and the metal ions present (concentration polarization effect).

As observed by Dolar et al. (2017) and Licona et al. (2018), the majority permeation mechanism in reverse osmosis membranes is of the sorptive-diffusive kind, so a high interaction between certain component(s) of the feed and the membrane is desired when an enriched permeate stream is desired.

in this component. On the other hand, a high chemical affinity of drugs with the membrane can facilitate their adsorption to it, generating a barrier to water permeation, which can explain the reduction in hydraulic permeability, especially in the permeation of feed solutions containing ibuprofen.

Rejection of drugs

The permeation tests showed that there was complete retention of ibuprofen and sodium diclofenac in all tests, regardless of the type of feed (whether alone or together) and the applied pressure, indicating that the membrane was efficient in generating a permeate current free of the drugs. Considering the quantification limits of the analysis method (0.15 $mg \cdot L^{-1}$ for DCF and 0.05 $mg \cdot L^{-1}$ for IBU), the minimum removal efficiencies of DCF and IBU were 98.5 % and 99.5 %, respectively.

Several studies in the literature report the use of reverse osmosis membranes for the removal of drugs and other pollutants that are difficult to treat in aqueous matrices, such as sanitary effluents, water from municipal sewage treatment, and surface water, among others. Table 3 lists some reverse osmosis studies for the removal of drug residues and other micropollutants and the removal efficiencies obtained.

Table 3 – Efficiency of removal of different drugs using reverse osmosis systems according to literature data.

Drug/substance	Removal efficiency (%)	Reference
Diclofenac	> 98.5 > 98.5 > 98.0	This work Snyder et al. (2007) Licona et al. (2018)
Ibuprofen	> 99.5 > 90.0 > 95.0	This work Lin (2017) Lin, Chiou, and Lee (2014)
carbamazepine	> 99.4	Snyder et al. (2007)
clofibric acid	87.0	Yangali-Quintanilla et al. (2008)
N-nitrosoamine	50.0 - 65.0	Plumlee et al. (2008)
Cyclophosphamide	90.0	Wang et al. (2009)
amoxicillin	99.4	Gholami et al. (2012)
Bisphenol A	87.0	Fatemeh et al. (2014)
Ibuprofen	98.0	Licona et al. (2018)
fluconazole	> 99.0	Couto et al. (2020)
Betamethasone	> 99.0	Couto et al. (2020)

Source: Authors (2023).

It can be observed that the results observed in the present study are like those found in the literature. Al-Rifai et al. (2011), for example, obtained 100 % efficiency of ibuprofen removal in effluents using reverse osmosis systems as tertiary treatment. The efficiency reported by Licona et al. (2018) for reverse osmosis in the removal of drug residues was above 98 %, considering the pH range of the feed between 4 and 7 and a transmembrane pressure of 10 bar. Linares et al. (2011) also observed IBU removal efficiency in the range of 99 % using reverse osmosis membranes as a treatment method.

The high removal efficiency, which was not influenced by the composition of the different feeds tested and did not change with the applied transmembrane pressure, demonstrates that there was no tendency to fouling. or concentration polarization, probably due to the low concentration of the tested drugs. However, as noted by Licona et al. (2018) and Lin, Chiou, and Lee (2014), the physicochemical conditions of the feed, such as pH, can cause changes in the structure or electrical charges of the substances present, which may increase or reduce the efficiency of their rejection by the membrane. In the case of IBU, which tends to partially ionize at neutral pH, unlike DCF, which is negatively ionized at pH > 4 (OH, SHIN; KIM, 2016; HU; LIU; KUAN, 2020), the interaction with the membrane may have been facilitated by only partial ionization, allowing electrostatic interaction, and by hydrophobic interactions. Hu, Liu, and Kuan (2020) commented that DCF tends to be adsorbed more easily at acidic pH (molecular form) than at neutral/alkaline pH (negatively ionized form), which may explain the complete rejection of this molecule, as well as the non-change in hydraulic permeability and transmembrane flow relative to distilled water permeation.

As cited by Lin, Chiou, and Lee (2014) and Licona et al. (2018), the removal of drugs and other micropollutants, when present in solution with other molecules, may be less effective due to interaction effects between the components of the feed and the membrane itself. Even so, the sorption and diffusion mechanism, which governs the reverse osmosis process, tends to be more restrictive, which facilitates the rejection of molecular species, such as drugs.

CONCLUSION

The reverse osmosis membrane used showed high efficiency in the treatment of feed solutions, with nearly complete removal (> 98.5 %) of the drugs IBU and DCF in the permeate stream, regardless of the type of feed, in all tests performed. Thus, the concomitant presence of both drugs in the feed solution had no deleterious effects on the membrane performance, which makes reverse osmosis even more interesting for the treatment of effluents containing these drugs and the presence of others. micropollutants.

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