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Intensification of diclofenac removal through supported liquid membrane and ozonation

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ABSTRACT

Pharmaceutical contaminants are frequently encountered at trace concentrations in various environmental ecosystems. This study introduces a significant approach to water treatment and environmental remediation by combining liquid membrane and ozonation. Initially, diclofenac is transported across the supported liquid membrane using a neutral organic extractant Cyanex 923. The highest removal efficiency was achieved with a 40 % concentration of Cyanex923 dissolved in kerosene, resulting in a permeability of 10.2 cm/h. Additionally, diclofenac is extracted from different environmental matrices such as tap water and real effluent of wastewater, and the effect of ions species was studied. The post-ozonation in the stripping phase resulted in removal of pharmaceuticals and 72 % reduction of total organic carbon at pH = 10 and 45.3 g/Nm^3 initial ozone concentration. The study also investigates the identification and tracking of the most prevalent by-product of diclofenac over time.

1. Introduction

Pharmaceuticals have been extensively used to prevent, cure, and treat diseases, and to increase life expectancy. However, the identification of pharmaceuticals in various environmental contexts has sparked significant health concerns. Numerous pharmaceutical agents are introduced into water sources, and their remnants are consistently identified in surface water, groundwater, wastewater, and even drinking water (Agüera et al., 2005). As these pharmaceutical substances remain essential to daily life, it becomes imperative to manage their consumption and discharge due to the potential risks they pose to both human well-being and aquatic ecosystems. Some pharmaceuticals, like antibiotics, can have detrimental effects on microbial genomes, leading to the development of bacterial resistance. One noteworthy pharmaceutical in this category is diclofenac, a nonsteroidal anti-inflammatory drug (NSAID) commonly used to alleviate pain and reduce inflammation. Diclofenac is considered one of the top-selling anti-inflammatory drugs and its oral global consumption was estimated at around 940 tons per year according to a trend analysis from, 2020–2027 for the consumption of pharmaceuticals (Alessandretti et al., 2021). Reygaert (2018) Furthermore, diclofenac can easily reach surface and wastewater through various means, such as improper disposal as solid waste, discharge through human and veterinary excretion, and effluents from industrial and urban wastewater treatment plants (WWTPs and UWWTPs). Conventional treatment methods have proven insufficient in removing diclofenac from water (Alessandretti et al., 2021). Recently, diclofenac has been detected in effluent

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water at concentrations up to 1.2 μg/L in various parts of Europe. Water undergoes conventional physical, chemical, and biological processes such as coagulation, flocculation, filtration, and disinfection (Rastogi et al., 2021). Yet several studies have addressed the low biodegradability of diclofenac and its high persistence in wastewater treatment plants, leading to its accumulation in surface waters, sediments, and sludge (Alessandretti et al., 2021; Rastogi et al., 2021). The partial or low elimination of diclofenac by conventional treatment has been reported by several studies: conventional coagulation and sedimentation (25 %) (Besha et al., 2017), membrane bioreactor 40 % (Patel et al., 2019), conventional activated sludge (66 %) (Miklos et al., 2018). In addition, the separation technique was studied to reduce the pharmaceutical environmental loading of pharmaceutical into the environment. The selective separation of diclofenac from urine was investigated with a strong-base anion exchange resin (Landry et al., 2015). However, over time, as the resin interacts with pharmaceutical compounds, it may become fouled or saturated, diminishing its capacity to effectively remove the target substances. Consequently, frequent resin regeneration or replacement might be necessary, resulting in increased operational costs and maintenance efforts. In addition, Ansarimehr et al. (2022) utilized solvent extraction with tetra-n-butyl ammonium bromide (TBAB) to extract diclofenac from water. Yet, compared to different separation techniques, solvent extraction techniques lack selectivity and can require additional separation steps (Ansarimehr et al., 2022).

Therefore, it is imperative to eliminate diclofenac from aqueous matrices to meet the required concentration levels. Various tertiary techniques have been developed for the removal of emerging contaminants, including adsorption, membrane separation, and advanced oxidation processes.

New advancements in membrane technology have significantly transformed wastewater treatment by improving pollutant filtration and extraction processes. The integration of membrane technologies in various applications, such as water treatment and desalination, has gained widespread popularity (Al-Hazmi et al., 2023). In contrast to conventional methods such as coagulation, flocculation, and biochemical treatments, membrane processes emerge as a highly efficient and promising approach for wastewater treatment. They not only save on chemicals and space but also provide superior treatment efficiency (Obaideen et al., 2022).

Membranes play a pivotal role as selective barriers in the separation and removal of contaminants at low concentrations. In this context, liquid membranes have been gaining widespread interest due to their high selectivity and simple manipulation. Unlike pressure-driven membrane technologies, liquid membranes (LM) operate based on the principles of facilitated transport and selective extraction (Kostanyan et al., 2023). By definition, LMs consist of an organic liquid phase immobilized within or supported by a porous material, typically a polymer support. This liquid phase acts as a carrier for specific substances, allowing them to be selectively transported or separated from one phase to another, such as from a feed solution to a stripping solution (Kostanyan et al., 2023; Malhotra and Ali, 2018). The driving force for separation does not come primarily from hydraulic pressure, but rather from the chemical interactions between the liquid membrane and the target components (Kostanyan et al., 2023; Malhotra and Ali, 2018).

Moreover, they can offer enhanced resistance to fouling and pore blockage compared to traditional solid membranes (Faramarzi et al., 2023; San Roman et al., 2010). As a result of these characteristics, liquid membranes have been used across different fields like environmental remediation, pharmaceutical purification, and chemical processing (San Roman et al., 2010). In particular, supported liquid membranes (SLM) are studied in various fields like analytical, chemical engineering, biotechnology, and biomedical engineering for the removal, pre-concentration, and recovery of targeted compounds (Balasubramanian and Venkatesan, 2012; Santiago-Santiago et al., 2012). They are mainly available in two forms flat sheet membranes (FSSLM) and hollow fiber (HFSLM). Lately, membrane processes, focusing on separation and extraction, can be integrated with advanced oxidation processes (AOPs) in several ways: as a pre-treatment to break down organic compounds in the feed stream, as a post-treatment for complete mineralization of non-rejected micropollutants in the permeate stream, or as a hybrid approach where both separation and degradation of pollutants are carried simultaneously (Ganiyu et al., 2015a). AOPs are defined by mainly the formation of hydroxyl radicals ($OH^{\cdot}$) with high oxidizing power capable of transforming complex organic compounds to other smaller molecules, carbon dioxide, water, and inorganic ions (Mussa et al., 2022; Qiu et al., 2020). Ozonation presents a unique feature that combines selective reaction with ozone molecules and unselective radical pathways with hydroxyl radicals to remove a wide spectrum of contaminants. The elimination of diclofenac by simple ozonation (Qiu et al., 2020) or with the addition of UV/H_2O_2 (Beltrán et al., 2009), activated carbon (Naddeo et al., 2012), sonolysis (Gao et al., 2017), catalytic ozone (Yaghmaeian et al., 2022), and Fenton-based processes (Othman et al., 2021) have been widely studied. The listed processes promoted mineralization but are faced with high energy costs, the formation of by-products, and the requirement of adding a disinfection final process (Ganiyu et al., 2015a).

AOPs are widely versatile and highly efficient for the abatement of various types of contaminants, yet they are less effective for the treatment of low-concentration pollutants and generate several toxic intermediates which at times are more harmful than the parent pollutants. AOPs usually request complementary treatments to remove such toxic byproducts that are generated alongside disinfection and oxidation effects. Numerous investigations have highlighted the viability and effectiveness of combining ozonation and membrane filtration to eliminate pharmaceutical and personal care products and their active by-products from water sources and wastewater (Kwarciak-Kozłowska, 2019; Ganiyu et al., 2015b). The majority of these studies focused on using ozone-based methods (O_3; O_3/H_2O_2 or O_3/UV) either as a preliminary stage before membrane filtration or as a post-treatment for both the filtrate and residue streams. For instance, Real et al. (2012) conducted a comparative study exploring the effectiveness of combining different chemical oxidation techniques, such as ozone (O_3), chlorine (Cl_2), ozone with hydrogen peroxide (O_3/H_2O_2), ultraviolet (UV) treatment and ultraviolet with hydrogen peroxide (UV/H_2O_2), with membrane filtration methods like ultrafiltration (UF) or nanofiltration (NF) to remove pharmaceutical compounds from water systems. The results confirm that using nanofiltration (NF) as an initial stage followed by ozonation was more effective in removing 97 % of pharmaceuticals from natural waters (Real et al., 2012). Nevertheless, Saquib et al. (2010) found that ultrafiltration (UF) used as a pretreatment with combined ozone and hydrogen peroxide had limited positive effects on removing organics from surface water (Saquib et al., 2010). Another study by Abdelmelek et al. (2011), examined the removal of diclofenac along with different types of pharmaceuticals RO retentate using ozonation (Abdelmelek et al., 2011). They monitored the

oxidation of organic matter in the retentate using excitation-emission matrix spectroscopy and were able to follow the evaluation of every contaminant used. Conversely, numerous research works have documented the practicality and effectiveness of membrane-catalyzed ozonation (Psaltou and Zouboulis, 2020), membrane filtration (Huang and Arning, 2019), or membrane-contact reactor systems for enhanced ozone dispersion and mass transfer (Peyrelasse et al., 2022). However, these methods often encounter challenges such as membrane fouling, energy consumption, chemical use, environmental concerns, and scalability issues. To provide an efficient tertiary treatment for the removal and degradation of diclofenac, liquid membrane technology with ozone treatment has been investigated. To the best of our knowledge, the integration of supported liquid membrane separation and ozonation within a single unit has not been explored. The primary objective of this study is to develop an efficient method to remove diclofenac from water with FSSLM coupled with ozonation. The focus is on achieving selective removal of diclofenac from the water stream during transport through the membrane and subsequent application of ozonation in the stripping phase. Initially, FSSLM was selected to gain a thorough understanding of the removal process of diclofenac from the feed to the stripping phase. Various operational parameters, including different organic extractant concentrations, environmental water matrices, and different initial ozone concentrations and the effect of oxone on the polymeric emmbranE were examined to measure the effectiveness of this process. Additionally, the generated by product during the ozonation were identified.This approach provides a preliminary and in-depth assessment of the potential combination of SLM with ozonation before transitioning to more complex configurations.

2. Materials and methods

2.1. Reagent and Chemicals

Diclofenac sodium salt (2-[(2,6-dichlorophenyl) amino] phenylacetic acid; CAS No. 15307–79–2) and its properties are listed in Table 1, and 5-hydroxydiclofenac ($C_{14}H_{11}Cl_2NO_3$) (2-[2-(2,6-dichloroanilino)− 5-hydroxyphenyl]acetic acid, CAS No. 62248) was supplied by Sigma-Aldrich. Fresh solutions were prepared with adequate concentrations (1, 10, and 30 mg/L) in deionized water at ambient temperature (25 °C). The chosen concentrations were intentionally higher than those typically encountered in actual water samples.to facilitate more accurate monitoring and measurement of the removal efficiency using the available analytical techniques. Acetonitrile, NaOH, KI, HCL and NaCl, were all obtained as high purity reagents from Merck. Potassium Indigo tri-sulfonate and potassium iodide were used for detecting residual ozone in the samples and were obtained from Sigma Aldrich.

2.2. Supported liquid membrane (SLM)

Cyanex 923 (Cy923, 94 %, Solvay), in the range of (0.126–0.757 mol/L) was selected to transport diclofenac after previously testing different organic extractants. The adequate concentration was diluted in commercial-grade kerosene. The diluent is known for its cost-effectiveness and low viscosity. The polymeric solid support used is Millipore polytetrafluoroethylene (PTFE). Further details regarding the membrane's specifications are provided in Table 2.

Transport experiments were conducted using an experimental set-up similar to the one depicted by a previous study (Farah et al., 2022). Solutions containing a specific concentration of diclofenac (DCF) were prepared using deionized water unless specified otherwise (such as real wastewater effluent or tap water). The permeation cell consists of two chambers (feed and stripping cell) of 220 cm^3 volume separated by the membrane. The PTFE membrane was submerged in a desired concentration of Cy923 in kerosene for a few minutes to effectively saturate the pores of the membrane with the organic extractant. Following this, the saturated membrane was carefully removed and thoroughly rinsed with distilled water to eliminate any excess Cy923, and placed between the chamber cells. In each cell, the feed, containing diclofenac at a pH of 5, and the stripping phase consisting of distilled water at a pH of 10, were introduced. The feed and stripping cells were mechanically stirred at 1000 rpm to minimize interfacial resistance, and they were maintained at a constant room temperature of 23 ± 2 °C. Throughout the experiment, the pH of both aqueous phases was continuously monitored using a Crison GLP21 pH meter and adjusted as necessary with a few drops of 1 M HCl in the feed phase and 1 mol/L of NaOH in the stripping cell. All experiments were conducted in replications for accuracy.

The transport of DCF across the membrane is based on the diffusion mechanism through the liquid membrane. It was assumed that the diffusion resistance on both the feed and stripping sides could be ignored. Additionally, the interfacial chemical reactions involving the formation of the DCF/Cy923 complex within the membrane, as well as its decomposition during the stripping process, were considered instantaneous. Consequently, the permeability coefficient of diclofenac, defined as the rate of transport through the membrane, was determined for various extractant concentrations (as per Eq. (4)). This calculation was accomplished by combining the fundamental concepts outlined in the first Fick law of diffusion (as represented by Eq. (1)) along with the mass balance of diclofenac in the feed (as detailed in Eq. (2))

Table 1
Pharmaceutical characteristics.

Compound	Diclofenac sodium salt
Molecular weight (g/mol)	318.1
Molecular formula	$C_{14}H_{10}Cl_2NNaO_2$
pk_a	4.15
Log $_{kow}$	4.51

Table 2
Specifications of PTFE support (Fluoropore™ FHLP04700).

Parameters	Value
Diameter (mm)	47
Pore diameter (μm)	0.45
Porosity (%)	85
Effective area (cm^2)	11.4
Thickness (μm)	150

$$J = -D\frac{dC}{dx} \approx -D\frac{\Delta C}{\delta * \tau} \tag{1}$$

Where J is the diffusive molar flux of DCF (mol /cm^2 h); D is the diffusion coefficient (cm^2/h); C is the concentration of diclofenac in the internal sides of the membrane (mol/L) and x is the position (m).

In addition, the mass balance of the pharmaceutical in the feed is given by the following equation:

Input + Generation – Output- consumption = Accumulation.

Accumulation = -Output.

Given there is no consumption, generation, or input, the accumulation is expressed as the rate of change of DCF over time in the feed and the output as the mass flow of transferred DCF to the receiving phase. The mass balance of DCF in the feed is expressed in (Eq. (2)):

Accumulation = - output

$$\frac{\mathrm{dmi}}{\mathrm{dt}} = \frac{\mathrm{VdC}}{\mathrm{dt}} = -\mathrm{N_{Out}} \tag{2}$$

With the mass flow, N_{out} (mol/h) is equal to the molar flux J (mol/cm^2 h) multiplied by the area of the membrane A (cm^2)

$$\mathrm{Nout} = \mathrm{J} * \mathrm{A} \tag{3}$$

Considering there is no accumulation in the membrane and combining (Eqs. (3) and (4)), the permeability coefficient is determined:

$$\ln\frac{C_t}{C_0} = -\frac{\mathrm{P}\cdot\mathrm{A}}{\mathrm{V}}\mathrm{t} \tag{4}$$

Given P is the permeability coefficient (cm/h), V volume of the feed (cm^3), A area of the membrane (cm^2), C_t and C_0 are the

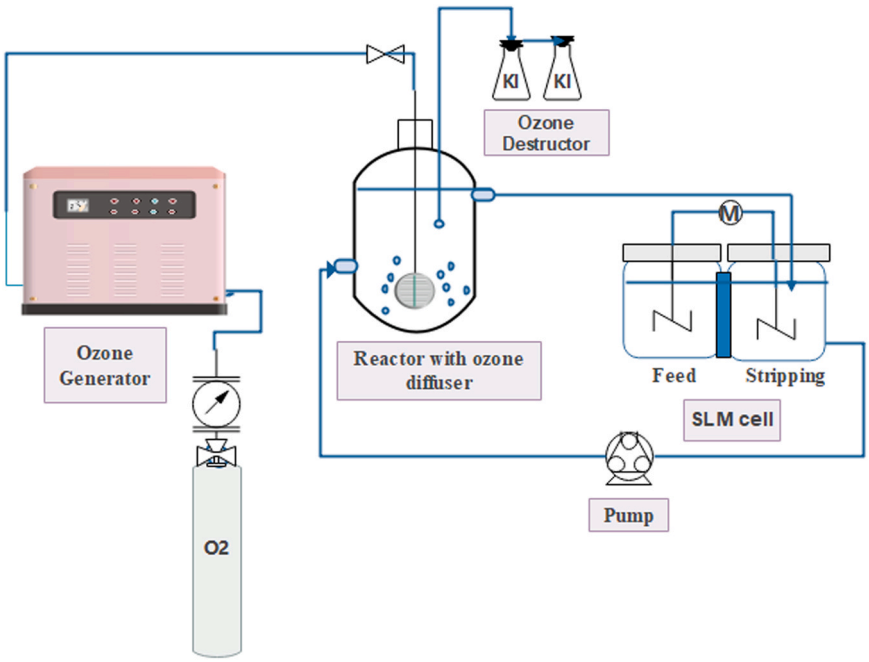

Fig. 1. Experimental set up.

concentration of diclofenac at a specific and initial time respectively and t the time (h) of the transport experiment.

2.3. Hybrid system: SLM and ozonation

Ozone was produced in situ by the Anseros ozone generator (COM-AD-04) at various initial ozone concentrations (10, 28.5, and 45.3 g O_3 /Nm^3) using pure oxygen. The flow rate was monitored with a flowmeter mounted on the Ozonator to regulate the feed gas entering the cell. Integrating ozone successively for the removal of pharmaceuticals from aqueous solution was conducted in a separate cell. Initially, ozone was initially introduced directly into the stripping cell of the FSSLM. However, this configuration was abandoned due to encountered issues where ozone diffused into the feed cell and caused undesired alterations of the polymeric support. It was observed that ozone diffused through the polymeric support and across the membrane from the stripping phase into the feed phase. Detailed information regarding the ozone diffusion through the PTFE membrane and the corresponding outcomes can be found in the supplementary materials. Alternatively, ozone was introduced in a separate cell as post-treatment to the flat sheet supported liquid membrane. Subsequently, it is applied after FSSLM, in a separate reactor to avoid any direct contact of ozone with the membrane surface. The feed was prepared using 10 mg/L of DCF dissolved in deionized water at pH = 5 and a volume of 220 cm^3. O_3 was continuously bubbled at a flow rate of 150 L/h through a diffuser placed at the bottom of the reactor at room temperature (23 ± 2 °C). The stripping phase (with a volume of 220 cm^3 and a pH of 10) was circulated in a closed loop within the ozone reactor using a peristaltic pump. Any excess ozone was removed by passing the solution through absorption bottles containing a 2 % (w/v) potassium iodide solution. The experimental scheme and setup are shown in Fig. 1. Samples were withdrawn from the feed and stripping cells at specific time intervals to evaluate the concentration of diclofenac.

2.4. Analytical method

The quantification of diclofenac transported across the membrane and the formation of its by-products was achieved using High-performance Liquid Chromatography (HPLC) on an Agilent 1100 Infinity series system equipped with a diode array detector set at 280 nm. The Zorbax C18 column (4 × 25 mm) was employed, and the mobile phase comprised a mixture of water and acetonitrile (60:40, v/v) with 25 mM formic acid (Huang and Arning, 2019). Meanwhile, the identification of transformation products was conducted using a Thermo Scientific™ Orbitrap IDXTribrid mass spectrometer with an ESI interface. The Vanquish UHPLC Liquid Chromatograph in line with a C18 column (4 × 25 mm) provided by Agilent was used. Elution was isocratically performed with a mixture of 25 mM formic acid (A) and acetonitrile (B) at a 60/40 (A/B) ratio, and the entire runtime was 15 min. The Mass spectrometry detection involved heated electrospray ionization settings in both negative and positive ionization modes. Additionally, pH measurements were taken both from the feed and stripping phase.

Total Organic Carbon (TOC) measurements at initial and final times were carried out utilizing a Shimadzu TOC-L model analyzer both before and after treatment.

The examination of the polymeric support structure before and after contact with ozone was conducted through scanning electron microscopy (SEM) with a field-emission scanning electron microscope (FEGSEM, Quanta 400F).

Finally, the concentration of dissolved ozone transported through the membrane was determined through its reaction with neutral potassium iodide, and the concentration of liberated triiodide was quantified at a wavelength of 352 nm using UV–visible spectrophotometer on a Lovibond XD 700 instrument.

3. Results and discussion

3.1. Diclofenac transfer in the FSSLM

By definition, the dissociation constant (pK_a) is used to determine the relative acidity or basicity of weakly ionizing compounds or their miscibility in aqueous solvent. The pK_a of DCF is 4.15, therefore at a pH lower than 4.15, the predominant species are the undissociated form of the contaminant: HA

$$HA \leftrightarrow A^- + H^+$$

Taking into account that Cy923 extracts neutral species, the pH of the dissolved diclofenac in water was measured to be approximately 5. As a result, the extraction process was conducted without making any adjustments to the pH in the feed solution. The organic carrier can solvate the undissociated form of the drug HA permitting the extraction of this molecule to the organic phase and the reaction equation for the extraction step:

$$\overline{Cy923} + HA \leftrightharpoons \overline{Cy923 \cdot HA}$$

The pharmaceutical substance forms a complex with the organic extractant and then moves through the membrane phase due to a concentration gradient. Eventually, it reaches the interface between the membrane and the product. At this point, the complex breaks apart due to the presence of hydroxide ions in the receiving phase. The reaction that takes place in the stripping phase is as follows:

$$\overline{Cy923 \cdot HA} + OH^- \leftrightharpoons \overline{Cy923} + A^- + H_2O$$

The performance is measured by calculating the permeability coefficient (cm/h) by combining the mass balance of solute in the

feed cell and the 1st Fick law of diffusion. The rate of transport of DCF was found to be 7.1 cm/h with 0.47 mol/L of Cy923 diluted in kerosene.

3.2. Effect of organic extractant concentration

To optimize the transport of pharmaceuticals the concentration of extractant was increased and the permeability was calculated. The results depicted in Fig. 2 show that a higher permeability was obtained with a greater concentration of Cy923 (0.975 mol/L). As shown in Fig. 2, an additional increase in Cy923 concentration has a noteworthy impact on permeability. This trend has been observed across various research papers that have explored the influence of extractant concentration on transport efficiency. In reality, the primary factors governing pharmaceutical transport are the diffusion coefficient and viscosity and they are related by the following expression (Pavón et al., 2020):

$$\text{Constant} = \mu^{\alpha} * D \tag{5}$$

Given D is the diffusion coefficient, μ is the viscosity of the mixture used.

Following the same procedure proposed by Pavón et al. (2020) and neglecting any extraction of diclofenac by the diluent (kerosene), the exact relationship between the permeability, the extractant concentration, and their related viscosity can be determined (Peyrelasse et al., 2022):

$$P_{DCF(\frac{cm}{h})} = 27.78 * [Cy923] * \mu^{-0.53.} \tag{6}$$

With αranging between 0.5 and 1 which is in accordance with several publications (Pavón et al., 2020; Hiss and Cussler, 1973) P is in (cm/h), [Cy923] in (mol/L), and μ in (mPa·s).

3.3. Effect of water matrices

The transport of DCF with flat sheet SLM and 40 % Cy923 as an extractant was tested in real environmental matrices. Tap water and wastewater treatment plant effluent samples were spiked with 10 mg/L of diclofenac and the pH was adjusted to 5. The operational conditions employed were identical to the ones in Section 3.1. The obtained results (shown in Fig. 3) demonstrate a slight increase in the permeability coefficient with both tap water and real wastewater effluent samples. The substantial presence of diverse ions in the actual water matrices can effectively enhance the elimination of diclofenac from aqueous solutions. On the other hand, Güell et al. (2010) tested the application of SLM system to remove arsenic acid from real water matrices, tap water, and river water. The results obtained indicated that the presence of various ions in the natural waters had no major differences in the values of permeability obtained (Güell et al., 2010). The variance in permeability obtained in the current study can be explained by the increase of the undissociated form of diclofenac in the feed which promotes the extraction with Cy923. Subsequently, the effect of varying concentrations of NaCl on the transport of diclofenac was investigated. SLM experiments were carried out by introducing a range of NaCl concentrations into the feed (from 0.2 to 1 mol/L), with 0.94 mol/L Cy923 as the organic extractant. The feed solution was maintained at a pH of approximately 5, while the stripping phase was set at 10.

As shown in the outcome of Fig. 3 the highest permeability coefficient was obtained with 0.1 M of NaCl in the feed. As a result, the ionic species within the feed solution can influence the efficiency of extraction. When considering the reactions of diclofenac and Cy923 in the aqueous phase, the equilibrium constant for the reaction can be expressed as follows:

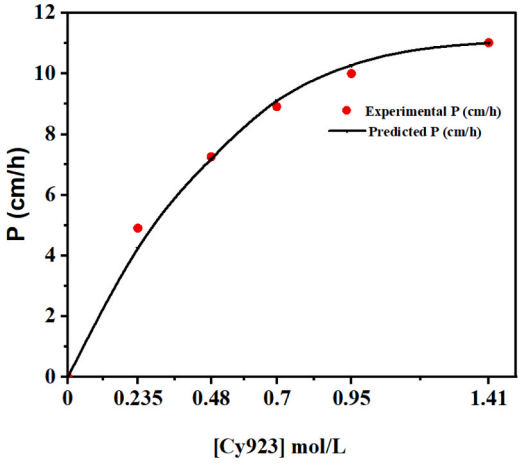

Fig. 2. Permeability coefficient for different concentrations of Cy923.

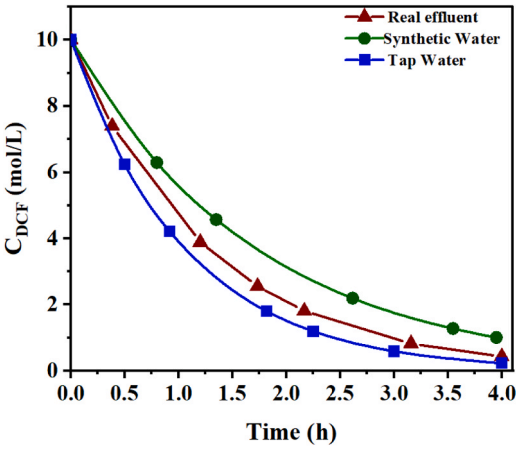

Fig. 3. Concentration of DCF in different water matrices.

$$k_{ex} = \frac{\overline{[Cy923{\cdot}HA]}}{[HA] * [Cy923]} \tag{7}$$

In addition, in non-ideal systems, the equilibrium description is expressed by the thermodynamic chemical equilibrium equation. Thus, the thermodynamic dissociation constant, expressed in terms of activities a_i of species i, are as follows (Minami and Kakiuchi, 2013):

$$Kc = \frac{a_{A^-} * a_{H^+}}{a_{HA}} = \frac{[A^-] * \gamma_{A^-} * [H^+] * \gamma_{H^+}}{[HA] * \gamma_{HA}} \tag{8}$$

Taking into account the acidity constant of diclofenac in water:

$$Ka = \frac{[A^-] \cdot [H^+]}{[HA]} \tag{9}$$

The equation relating the ionic strength (Eq. (10)) and the dissociation constant is obtained by combining (Eq. (8) and (9)):

$$Kc = Ka \cdot \gamma_{A^-} \cdot \gamma_{H^+} \tag{10}$$

According to Davies equation, after the addition of ionic species, the ionic strength increases whereas the activity of species decreases (Bird, 2002). Taking into account that Kc is a constant (Eq. 10), the dissociation of diclofenac will increase to maintain a constant value. Hence, the concentration of undissociated diclofenac in the feed solution will be higher, thereby enhancing the extraction process with Cy923. As shown, the transport of DCF increased with the concentration of sodium chloride in the solution where the permeability with 40 % (v/v) Cy923 was found to be 28 cm/h with 0.1 M of NaCl in the feed The results obtained are in accordance with the previous studies for the extraction of metals, phenols and batteries chemicals with Cy923 (Dewulf et al., 2020). (Fig. 4).

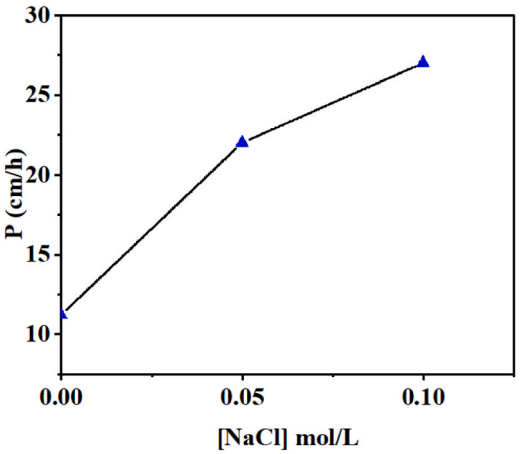

Fig. 4. Effect of NaCl concentration on the permeability coefficient.

3.4. Hybrid system: SLM and ozonation

Ozone is a powerful oxidant that potentially reacts with various organic compounds. It is a well-established technique for wastewater treatment, disinfection, odour, and colour removal (Mansas et al., 2020).

The decomposition reaction of ozone yields two molecules of hydroxyl radicals via a radical chain reaction:

$$3O_3 + HO^- + H^+ \rightarrow 2HO^\bullet + 4O_2$$

Diclofenac is can be oxidized either through the direct reaction with ozone molecules or indirectly with hydroxyl radicals to produce by-products depending on the operational conditions adapted in the treatment process:

$$O_3 + DCF \rightarrow BP + O_2^{\cdot}$$

$$HO^{\cdot} + DCF \rightarrow BP + HO_2$$

While ozone has proven to be an effective and environmentally friendly method for water treatment, it is constrained by its limited mass transfer in water, often necessitating a substantial surface area for contact. This can result in high energy consumption and operational requirements (Prada-Vásquez et al., 2021; Huber et al., 2005). In fact, a recent review has highlighted the substantial cost of ozone, which can reach as high as $346 per day for a water treatment plant with a capacity of 0.38 hm^3/day (Mundy et al., 2018).

However, the integration of FSSLM prior to ozone treatment offers a promising solution. SLM enhances the preconcentration potential for compounds like diclofenac and increases the selectivity of oxidation towards this specific pharmaceutical, minimizing the need for extensive ozonation. This innovative approach not only improves the overall efficiency of the treatment process but also significantly reduces the consumption of ozone, making it a more cost-effective and sustainable solution for pharmaceutical pollutant removal in water treatment.

To address the challenges linked to ozonation techniques and improve the breakdown of diclofenac, a selective transport method using a liquid membrane as described in previous sections has been integrated as a prior step to the disinfection phase with ozone. The primary aim of this study is to extract the diclofenac that remains after conventional treatment and subject it to ozone treatment to encourage its breakdown and the mineralization of both the primary product and any by-products formed. The goal is to combine these two treatments in a mode to optimize membrane specifications and performance with minimal impact and alteration. Hence implementing ozone in separate cells.

Up to the present day, the most prevalent approach for employing ozonation in conjunction with polymeric membranes is as an alternative method for enhancing gas-liquid mass transfer (Bamperng et al., 2010). These membranes serve as inert, permeable barriers between the liquid and gas phases. However, the scalability of ozone membrane contactors has often been hindered by the stability of polymeric membranes when exposed to ozone molecules over extended periods. It's crucial to consider the potential for material alteration after prolonged exposure to ozone.

Direct contact of ozone with the PTFE polymeric membrane is discarded for several reasons but mainly to avoid any modification in the membrane specifications. In fact, the performance of both PVDF and PTFE polymeric support after exposure to ozone was investigated to treat dye wastewater (Bamperng et al., 2010). The results obtained confirm that these membranes can enhance the dissolution of ozone in water however the alteration of their surfaces cannot be avoided (Bamperng et al., 2010; Santos et al., 2015) In addition, the lifetime of polymeric membranes is estimated to be between one and five years with high exposure to ozone (Mundy et al., 2018). To confirm the statement with the published studies, the surface of PTFE membrane in direct contact with ozone after 6 h, was examined and the scanning electron micrographs of its outer surface are shown in Fig. 5. As shown from the outer surface morphology, no significant modifications were noticed, thus the membrane exposed to ozone exhibits more stretched pores compared to the intact membrane. It is well known that the wider the pore diameter the more is probable for the organic extractant to leach out from the membrane.

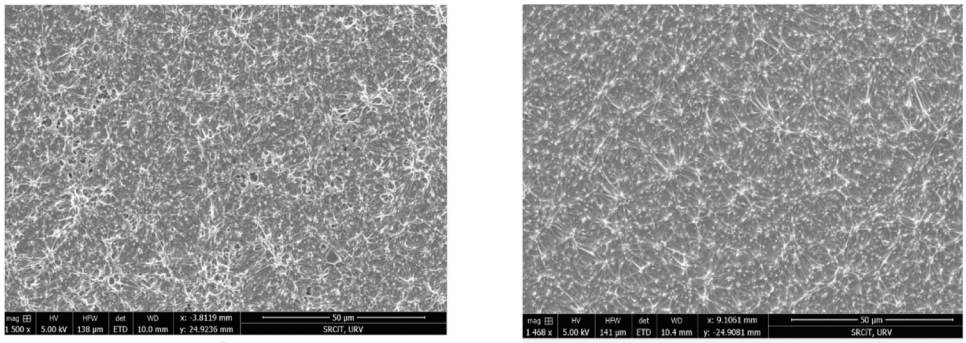

Fig. 5. SEM images of PTFE membrane surface: (a) Ozone exposure; (b) Intact membrane.

3.5. Transport of DCF in SLM at different ozone concentrations

Experiments were conducted following the experimental setup illustrated in Fig. 1. In this setup, 10 mg/L of diclofenac was transported from the feed at pH = 5, to the stripping phase with a pH= 10 using 40 % Cy923. The stripping phase was continuously recirculated into the ozone reactor, where three different initial gas flow rates were tested. The results shown in Fig. 6 illustrates the changes in diclofenac (DCF) concentration over time in both the feed and the stripping phase.

Ozone is decomposed to produce $OH^{\bullet}$ radical at basic conditions. The reaction of diclofenac with $OH^{\bullet}$ radical is very fast and therefore the diclofenac transported through the membrane was completely eliminated in less than 1 h for all three different initial ozone concentrations. Concerning the feed phase, the transportation of DCF using this method appeared to be similar to the process without applying ozone, and the permeability coefficient was found to be 10.2 cm/h. According to research by Huber et al. (2005) achieving complete oxidation and degradation of DCF through ozone treatment requires a minimum molar ratio of ozone (O_3) to diclofenac of approximately 10:1 (Bamperng et al., 2010; Coelho et al., 2009). Therefore, it's crucial to ensure a sufficient supply of ozone to effectively remove pharmaceutical contaminants and their by-products from the solution.

To evaluate the effectiveness of this treatment, total organic carbon (TOC) levels were measured in both the feed phase and the stripping phase before and after the 4-hour experiment. Notably, the highest TOC removal rates were achieved when the initial ozone concentration was 45.3 g/Nm^3, with more than 83 % TOC removal observed in the feed phase and 72 % in the stripping phase. This indicates a substantial reduction in organic carbon content in the water.

Following these experiments, the oxidation with ozone, following a selective transport process involving 10 mg/L of DCF, led to a significant level of mineralization after three hours. However, it's important to note that the disappearance of the target pollutant alone does not necessarily indicate the success of a water treatment method. In many cases, the by-products generated during treatment can be even more harmful than the original pollutant. Therefore, the identification of by-products is conducted.

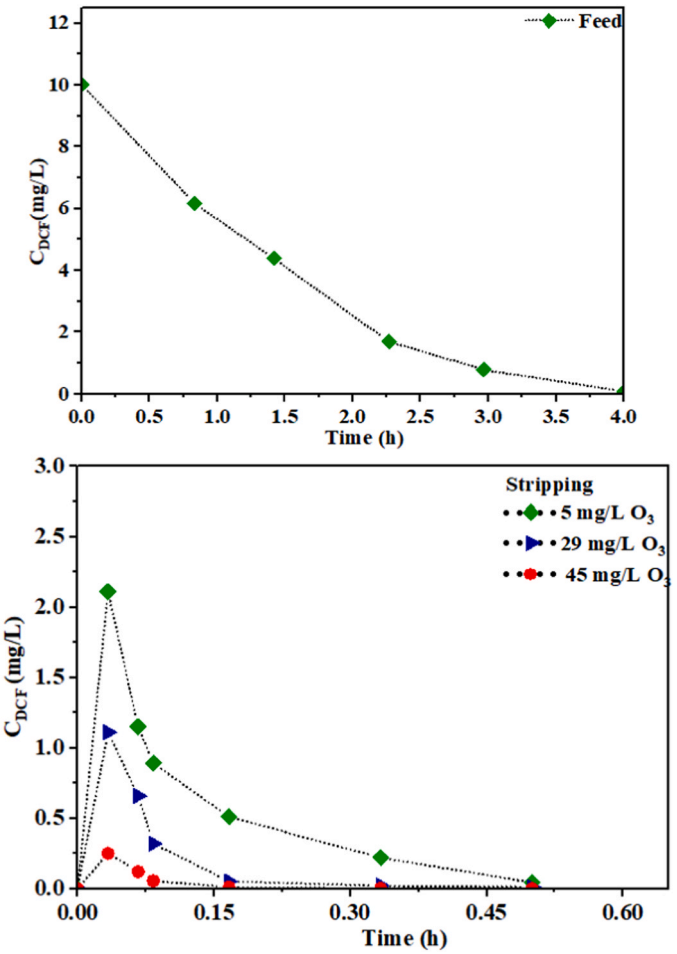

Fig. 6. Concentration of Diclofenac in the feed and stripping cell in the hybrid system.

3.6. By product Identification

Complete removal of the Diclofenac transported through the membrane resulted in the identification of 9 by-products when applying ozone in a separate cell. High-resolution MS data for the identified by-products containing the measured and exact mass of the detected molecular ions are shown in Table 3.

Ozonation of DCF in the stripping phase at basic conditions mainly involved hydroxylation reaction. The addition of hydroxyl groups in this case is indirectly via a hydroxyl radical produced from the reaction of ozone in an aqueous solution (Santos et al., 2015; Coelho et al., 2009; Monteagudo et al., 2018) The results obtained in Table 3 confirm the hydroxylation of DCF through the increase of one or more oxygen atoms with respect to DCF molecular. Although the reaction of the pharmaceutical with ozone molecules needs to be taken into consideration, including O_3-addition at different sites of two benzene rings and amino groups of diclofenac (Mundy et al., 2018; Bamperng et al., 2010) have been investigated. The evolution of by-products shifts during the reaction as some compounds decrease while new ones are formed. Initially, D1 (5 hydroxydiclofenac) was found in greatest abundance indicating that the DCF degradation is initiated by the hydroxylation of the phenylacetic ring. 5-hydroxydiclofenac was identified and analysed and the evolution of its concentration is shown in Fig. 7.

The primary by-product of diclofenac was successfully identified and quantified. The highest concentration of this by-product, referred to as D1, was observed at high ozone concentrations reaching 0.35 mg/L with an initial DCF concentration of 10 mg/L. This trend aligns with previous findings reported by several studies that investigated the degradation of diclofenac under various ozone concentrations (Huber et al., 2005; Kråkström et al., 2021). It's worth noting that diclofenac's degradation with ozone can follow different pathways depending on the operational conditions.

D1 is a commonly detected and quantified by-product of diclofenac in such processes. Interestingly, after three hours, the concentration of D1 decreased significantly, reaching a minimum value when the solution was recirculated in the ozonation reactor. Moreover, the results of TOC after three hours of experimentation revealed a 72 % decrease compared to its initial value (10 mg/L DCF). This outcome suggests a promising application of supported liquid membranes for selectively transporting and preconcentrating streams containing emerging pharmaceutical contaminants. Subsequently, these contaminants can be effectively degraded with continuous exposure to ozone.

However, it's crucial to highlight the importance of conducting toxicity assessments to measure the potential harm caused by these by-products. This information is vital for making informed recommendations regarding the safety and suitability of this treatment method in real-world applications, particularly with respect to environmental and human health.

4. Conclusion

The emerging of pharmaceutical contaminants and especially antibiotic residues in the environment is a crucial complex that requires more upgraded waste water treatment technologies. The majority of conventional technologies are limited by their removal efficiencies, high operation costs, and increased energy consumption.

In this study, supported liquid membrane coupled with the oxidation method was evaluated as an alternative effective method for the removal of pharmaceutical diclofenac and its degradation products. The feasibility of the hybrid process was tested in a laboratory-scale flat sheet membrane in order to scale it up for a preconcentration and using the hollow fiber modules.

Diclofenac was transported through the liquid membrane with 0.94 mol/L equivalent to 40 % (v/v) Cy923 at a transfer rate of 10.2 cm/h. and the equation to predict the permeability coefficients for DCF depending on the Cy923 concentration and the organic phase viscosity was calculated. Supported liquid membrane was tested with real water matrices and the removal of pharmaceutical contaminants was not influenced by the presence of counterions. Following that, ozone was applied to react with the extracted pharmaceutical to achieve a high degree of mineralization. The main contaminants were removed after three hours. The reaction of diclofenac with ozone generated 9 by-products and the formation of 5-hydroxydiclofenac was identified and quantified. The proposed approach leads to the additional removal of DCF and its intermediate compounds while preventing any contact of membrane materials with ozone molecules. Supported liquid membrane are simple and low cost methods that can be successively integrated with well-established technologies like ozone for water treatment.

CRediT authorship contribution statement

Frank Stüber: Writing – review & editing. **Azael Fabregat:** Writing – review & editing, Project administration, Supervision. **Agustín Fortuny:** Supervision, Writing – review & editing, Conceptualization, Formal analysis, Methodology. **Josep Font:** Funding acquisition, Writing – review & editing. **Jaume Giralt:** Writing – review & editing. **Mary Farah:** Writing – original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Table 3
Identified by-products with LC-MS in positive and negative mode.

Compound	High-Resolution Ms data Exact measured Molecular ion $[M-H]^-$	Molecular Weight (g/mol)	Retention time (min)	Molecular Formula	Reference
DCF	296.02	295.01	10.4	$C_{14}H_{12}NO_3Cl_2$	(Coelho et al., 2009; Monteagudo et al., 2018; Alharbi et al., 2022)
D1	311.02	312.01	3.7	$C_{14}H_{12}NO_3Cl_2$	(Coelho et al., 2009; Monteagudo et al., 2018; Alharbi et al., 2022)
D2	308.99	310.01.	2.94	$C_{14}H_{10}NO_3Cl_2$	(Coelho et al., 2009; Monteagudo et al., 2018; Alharbi et al., 2022)
D3	327.01	328.13	1.46	$C_{14}H_{12}NO_4Cl_2$	(Coelho et al., 2009; Alharbi et al., 2022)
D3a	327.01	328.13	1.74	$C_{14}H_{12}NO_4Cl_2$	(Coelho et al., 2009; Monteagudo et al., 2018; Alharbi et al., 2022)
D5	284.99	286.01	3.0	$C_{12}H_{10}NO_3Cl_2$	(Coelho et al., 2009; Santos et al., 2015)
D6	281.0	282.01	1.62	$C_{13}H_{10}NO_2Cl_2$	(Coelho et al., 2009; Monteagudo et al., 2018; Alharbi et al., 2022)
D7	277.05	278.11	1.62	$C_{14}H_{10}NOCl_2$	(Coelho et al., 2009; Monteagudo et al., 2018; Alharbi et al., 2022)
D8	296.99	298.01	3.05	$C_{13}H_{10}NO_3Cl_2$	(Coelho et al., 2009; Monteagudo et al., 2018; Alharbi et al., 2022)
D9	258.97	259.99	1.39	$C_{10}H_8NO_3Cl_2$	(Monteagudo et al., 2018; Alharbi et al., 2022)

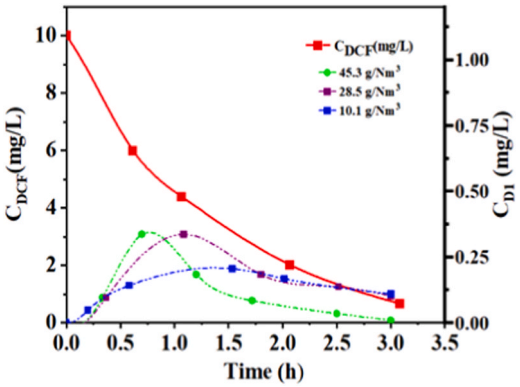

Fig. 7. The evolution of DCF in the feed and D1 concentration in the stripping with time at different initial ozone gas concentrations.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.eti.2023.103469.

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