Supported liquid membranes for the removal of pharmaceuticals from aqueous solutions

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ARTICLE INFO

ABSTRACT

In the following study, the extraction of three pharmaceutical compounds: Diclofenac (DCF), ibuprofen (IBP), and carbamazepine (CBZ) by liquid-liquid extraction and their transport by supported liquid membrane (SLM) using different commercial extractants (Cyanex 923 (Cy923), trioctylamine (TOA), tributylphosphate (TBP), and Versatic Acid 10 (neodecanoic acid)) were evaluated.

Cy923 was demonstrated to be an efficient extractant for diclofenac and ibuprofen removal through a facilitated transport mechanism from the aqueous feed phase to the aqueous stripping phase using hydroxide ions as stripping agent. Around 80 % of these pharmaceuticals were extracted in 4 h with 10 % of Cy923 and without extreme alteration in the pH. As for carbamazepine, the stripping conditions were achieved with 10 % of Versatic Acid 10. Variation of concentration of different extractants indicates that a higher transport of diclofenac can be obtained by using 40 % of Cy923. In addition, two commercial polymeric supports (PTFE and PVDF) were compared for the selected operational conditions. Finally, the lifetime of the membrane was extended by soaking the polymeric material in the organic solution under vacuum for 24 h and compared with the membrane prepared with an ultrasound-assisted method. Supported liquid membranes present many advantages and can easily be manipulated and integrated for the treatment of persistent pharmaceutical contaminants from water.

1. Introduction

Among the large number of pollutants that occur in the environment, the presence of pharmaceutical contaminants is recognized as an issue of major concern. The escalation in medication use is associated with the continuous growth of population, life span, new diseases, climate change, and pharmaceutical industry expansion. In fact, pharmaceutical usage in Germany is projected to increase by 43 to 67 % by the year 2045 [1]. Despite being essential for human and animal health, pharmaceutical residues and their active compounds are detected in the aquatic environment, surface water, groundwater, and drinking water. One of the major reasons, that these contaminants are gaining great attention, is their ability to interact with a living system and produce a pharmacological response even at low doses. For instance, the excessive use of antibiotics can cause antimicrobial resistance as well as psychiatric drug residue can alter fish behaviour and endocrine-disrupting pharmaceuticals can cause reproduction toxicity in fish and increase the risk of breast or prostate cancer in humans [2].

Many pharmaceutical residues are non-biodegradable and resistant to conventional wastewater treatments. The impacts of pharmaceuticals in the environment depend on a combination of variables, including the toxicity, degradation, persistence, and properties of the drugs [3]. Therefore, it is necessary to upgrade the existing conventional wastewater treatment technologies to be able to cope with new emerging contaminants and their metabolites even at low concentrations, taking into account the potential for energy savings [4,5].

Various methods have been proposed to remove pharmaceuticals from the aquatic solutions such as adsorption [6,7], advanced oxidation processes (AOPs) [8], biological treatment [9], membrane filtration [10], and were intensively investigated for industrial applications and abatement of various organic pollutants. Notwithstanding their wide range of applications, these techniques are limited by their low efficiency at low contaminant doses, sensitive operating costs, production of secondary sludge, and disposal requirements. Common technologies such as conventional biological treatment are efficient for a limited number of compounds. Other pharmaceutical compounds show a remarkable persistent behaviour, such as carbamazepine, which is neither sorbed, nor biotransformed and diclofenac is partially removed.

Membrane technologies namely reverse osmosis, microfiltration, ultrafiltration, electrodialysis are used successfully in the separation, recovery, and removal of various organics and inorganics from wastewater plants [11,12]. When the concentration is relatively low (ng/L–µg/L) (pharmaceutical active compounds, endocrine disrupting compounds, and artificial sweeteners), liquid membranes are considered the optimum alternative solution for their removal. Liquid membranes combine extraction and stripping in a single unit which is separated by a thin film of the organic phase, permitting selective mass transfers of gases, ions, or molecules to occur via permeation and transport processes. Characterized by high selectivity, operational simplicity, low solvent inventory, and low energy consumption, liquid membranes present pronounced advantages over the traditional separation methods [13]. Henceforward, they have been given considerable attention all over the world ever since they were discovered by Li and co-workers in 1960, they have been used for various purposes such as the recovery of metal ions from aqueous solutions, the removal of contaminants from industrial effluents, and the recovery of fermentation products. To this end, three different types of liquid membranes: emulsion liquid membranes (ELM), bulk liquid membranes (BLM), and supported liquid membranes (SLM) were used for separation studies. They differ by the mode in which the carrier is retained in the membrane [14]. Basically, the concept of all liquid membranes consists of an extractant agent (carrier) in the organic solvent that binds with high selectivity to one or a class of components in the aqueous feed phase and transports it to the aqueous receiving phase (stripping) through the membrane. Supported liquid membranes (SLMs) are non-dispersive liquid membranes where the organic solvent is immobilized in the pores of a hydrophobic polymer. These varieties of liquid membranes do not depend on the conditions of equilibrium and aqueous/organic phase ratio which are the main setbacks of membrane processes. They can be categorized as flat sheets or cylindrical types based on their size, shape, surface area, and applications.

SLMs systems have been adapted in both industrial and analytical fields for separation, preconcentration, and wastewater treatment. SLMs have been extensively used for the recovery of metals from industrial process streams. Several authors have reported the recovery of metal and anions such as copper, zinc, nickel, Cr (VI), Hg, and cadmium through liquid membrane contactors [15–18].
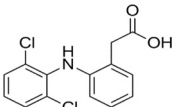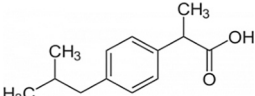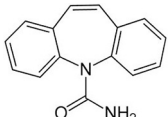
In the last years, more studies were conducted on implementing SLMs for the separation of fine chemicals and even drugs from wastewater. Evidently, their ability to extract products in relatively small volumes makes SLM technology even more attractive to the pharmaceutical industry as an alternative solution for distillation, crystallization, solvent extraction, and precipitation [19]. On this basis, membrane techniques and more specifically supported liquid membranes are the optimal choices that check all the requirements for an efficient treatment to remove pharmaceutical contaminants from water [20].

The removal of ibuprofen (IBP) and its metabolite 4-isobutylacetophenone (4-IBAP) was investigated by Williams et al. in a flat sheet and hollow fiber membrane using canola oil as a non dispersive organic extractant [21]. The removal efficiency was about 90 % in the first 15 min for ibuprofen and its metabolite. Acetaminophen an antipyretic and analgesic drug, was extracted as well by bulk liquid membrane with ionic extractant Aliquat 336 [22]. In this research, the initial feed phase concentration, stripping phase, concentration of NaCl, temperature, pH, the volume ratio of feed phase to membrane phase, agitation speed, carrier concentration, solvent type were varied to select the best conditions and high extraction efficiency of 97 % was achieved at the best experimental conditions [22].

Lately, the drugs most frequently detected in wastewater are anti-inflammatories, antibiotics, hormones, lipid regulators, anticonvulsants, anti-ulcer agents, diuretics, antidiabetics, and bronchodilators [23]. Diclofenac([2-(2,6-Dichloroanilino)phenyl]aceticacid) and ibuprofen (methylpropyl)phenyl)propanoic acid) are typical representatives of analgesic non-steroidal anti-inflammatory pharmaceutical compounds (NSAIDs).these types of drugs are easily accessible and sold

Table 1
Pharmaceutical compounds chemical structure.

Compound	Molecular structure	MW (g/mol)	pKa
Diclofenac		296.14	4.15
Ibuprofen		228.26	4.9
Carbamazepine		236.37	13.9

Table 2
Characteristic of polymeric membranes.

Material	Polyvinylidene fluoride PVDF (Millipore Durapore GVHP 10)	Polytetrafluoroethylene film PTFE (Fluoropore FHLP04700, Merk)
Pore diameter (µm)	0.45	0.45
Porosity (%)	75	85
Thickness (µm)	125	150[a]
Effective area (cm²)	11.4	11.4

[a] Including 100 µm of the polyethylene grid.

over the counter [19].Traces of diclofenac are found in the effluent of water and was listed in the European first watch substances list [23] and for ibuprofen was found in sewage treatment plants effluents and surface water at concentrations ranging from 600 to 85,000 ng/L in parts of Europe, Canada, and USA [9,13–23]. In addition to anti-inflammatory, the emergence of psychiatric drugs in drinking water has garnered a lot of scientific interest, particularly with regard to the effects of long-term exposure. Carbamazepine (5H-dibenzo[*b*,*f*]azepine-5-carboxamide) is a common pharmaceutical prescribed for antiepileptic and the treatment of neurotic pain seizure disorders and several psychological disorders [23].

In the following study, flat sheet supported liquid membranes (SLM) are investigated for the separation of drugs (diclofenac, ibuprofen, and carbamazepine) from aqueous solution in laboratory-scale chambers. Different operational parameters, types of extractants, transfer time, and polymeric support were analysed in order to select the optimum conditions for the transport of different pharmaceutical contaminants from water streams. Finally, the stability of the supported liquid membranes is tested.

2. Material and method

2.1. Reagents

Diclofenac sodium salt (D6899) ibuprofen sodium salt (I1892) and carbamazepine (C4024) were purchased from Sigma Aldrich. The chemical structure of each pharmaceutical is shown in Table 1. Stock solutions of drugs (30 mg/L) were prepared in deionized water.

2.2. Supported liquid membrane

The components of the SLM system, namely support, extractants and diluent have been made for the laboratory grade. The solid support in a

Table 3
Range of concentration of extractants used.

Extractant	% v/v
Kerosene with no extractant	–
Cyanex 923 in kerosene	10, 20, 30, 40, 60
TBP in kerosene	20, 40, 80
TOA in kerosene	5; 10, 20
Versatic Acid 10 in kerosene	10
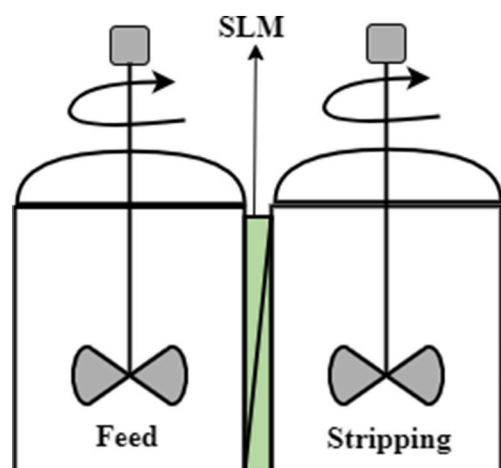
Fig. 1. Schematic representation of the experimental setup.

supported liquid membrane is a hydrophobic polymer that can retain the organic solvent in the membrane pores by capillary action. Two different types of polymers were used and their specifications are presented in Table 2.

The pores of the membrane were filled with an organic solvent based on the selectivity of the components present in the feed phase. Cyanex 923 (Cy923, 94 %, Solvay), trioctylamine (TOA, 98 %), tributylphosphate (TBP, 99 %, Merk), methyl (trioctyl/decyl) ammonium chloride quaternary amine (Aliquat 336, 90.9 %) and a neodecanoic acid (Versatic Acid 10, 98 %) were tested for exaction of pharmaceutical compounds. All extractants were diluted in kerosene to be a cheap diluent with low viscosity and solubility. The different concentrations of organic extractants are summarized in Table 3.

2.3. Extraction test procedure

Liquid-liquid extractions (L-L) for the three pharmaceuticals were carried out in a small beaker where 5 mL of the aqueous solution containing 30 mg/L of contaminants is mixed with 5 mL of organic phase at room temperature 23 ± 3 °C. The two phases were stirred at 200 rpm for 1 h. Afterward, the solution was put to rest in a separatory funnel for 10 min to separate the phases. The aqueous phase was separated and the concentration of the drug remaining was analysed by high-performance liquid chromatography (HPLC, Agilent 1100 infinity series) with a diode array detector at 280 nm, 230 nm, and 285 nm for diclofenac, ibuprofen, and carbamazepine respectively. The column used was Hypersil C18 (4 × 25 mm) and the mobile phase consisted of a mixture of formic acid (25 mM) in water and acetonitrile at 60:40 (v/v) with a flow rate of 1.0 mL/min. The concentration of pharmaceuticals in the loaded organic phase was determined by the mass balance of the pharmaceutical before and after extraction. The main purpose of conducting L-L extraction is to select the optimum conditions of extraction and stripping for the transport studies. The pH values of the aqueous solutions were varied from 2 to 13 and the initial and equilibrium pH values were measured with a digital pH meter GLP 21.

2.4. Supported liquid membrane preparation and transport experiment

The supported liquid membrane was prepared by soaking the polymeric support into the organic extractant (5 mL) listed in Table 3 for few minutes. Based on preliminary results, long immersion time was not required since the contact time for the membrane with the organic extractant was sufficient to saturate the membrane pores. The liquid membrane was then removed, wiped with a soft paper to eliminate the excess solution, and inserted into the permeation cell shown in Fig. 1. The permeation cell consists of two chambers (feed cell and stripping) of 220 cm^3 each, communicated with a circular window where the impregnated membrane is placed. Following that, the stripping phase composed of water at basic conditions and the feed phase composed of 30 mg/L of pharmaceutical dissolved in deionized water were added respectively in each cell and stirred mechanically at 1000 rpm at room temperature (23 ± 2 °C). The pH of both phases was continuously monitored during the experiment and was adjusted when needed to the operating value by adding some drops of 1 M HCl in the feed and 1 M NaOH in the stripping cell.

Batch experiments were carried out for pharmaceutical transport (diclofenac, ibuprofen and carbamazepine) with the different organic extractants. At established time intervals, aliquots were withdrawn from the feed and stripping cells, and the concentration of pharmaceuticals was measured as described previously in Section 2.3.

The rate of transport and the quantity of transported solute through a specific area of the membrane into a given unit time for different operational parameters are usually defined by the permeability coefficient P. The permeability is derived from the mass balance of solute in the feed cell and Fick's law of diffusion (Eq. (1)).

$$ln\frac{C_t}{C_0} = -\frac{P \cdot A}{V}t \tag{1}$$

where P is the SLM permeability (cm/h), C_t and C_0 are the concentration of the studied pharmaceutical at time t and at time 0 respectively, A is the SLM area (cm^2), V is the volume of feed phase (cm^3) and t is the time in hours.

2.5. Stability of SLM

SLM provides different advantages and yet they are rarely implemented at industrial scale due to their short lifetime and their instability [11]. This very much depends on different factors such as the nature of solvent used, the type of polymeric support and the pore size. Firstly, the stability of both PVDF and PTFE polymer supports were tested by conducting transport experiment for diclofenac for three consecutive runs of 3 h. The liquid membrane phase was drenched with a 40 % solution of Cyanex 923 in commercial kerosene. Secondly, to improve the lifetime of the membrane, the pores of PTFE polymeric support were filled with the organic solution of Cy923 40 % (v/v) in two ways: Under vacuum pressure for 24 h and at atmospheric pressure but assisted by ultrasound (50 kHz, 150 μm) for 30 min. by means of ultrasonic Lab homogeniser UP200S M (Hieltcher). The active layer of the polymeric support was positioned perpendicularly to the direction of the ultrasound and at a distance of 10 mm from the ultrasound probe. Transport studies were carried out for 3 h by monitoring the concentration of diclofenac in the feed phase.

3. Results and discussion

3.1. Extraction tests

Liquid-Liquid extraction experiments were studied primarily to define the best-operating conditions to be used in the transport studies. The effects of pH in the extraction extension for the different organic extractants used were investigated for each pharmaceutical. Samples
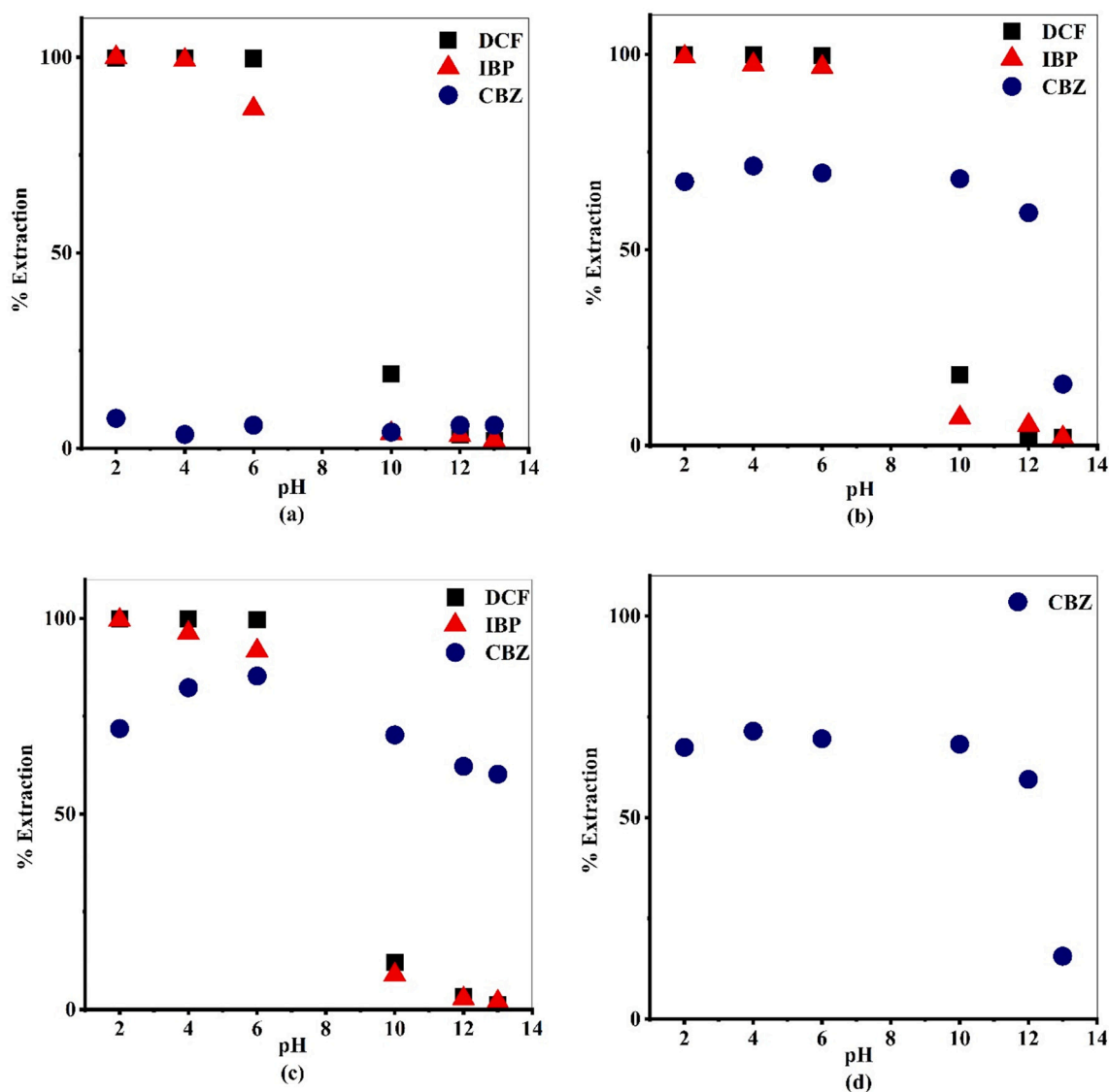
Fig. 2. Effect of the pH$_{equilibruim}$ on the extraction of pharmaceuticals with different extractants: (a) 10 % TOA; (b) 20 % TBP; (c) 10 % Cy923; (d) 10 % Versatic Acid 10.

with 30 mg/L of diclofenac (DCF), ibuprofen (IBP) and carbamazepine (CBZ) were prepared in a range of pH between 2 and 13. 10 % (v/v) of Cy923, 20 % (v/v) TBP and 10 % (v/v) TOA diluted in kerosene were used to estimate the distribution coefficient and the extraction efficiency with V$_{aqueous}$/V$_{Org}$ = 1. All extractants were diluted in kerosene.

The extraction results corresponding to the type of extractant obtained at equilibrium pH are shown in Fig. 2a, b, c and d. As expected for both carboxylic acid compounds (DCF and IBP), they are extracted simultaneously and completely at acidic pH with Cy923, TOA, and TBP. Upon analysis of the diclofenac, it was noticed then for a pH <4, the initial concentration of diclofenac exhibited a decrease (the measured concentration obtained was 20 mg/L lower than the concentration at neutral pH 30 mg/L) caused by the formation of insoluble diclofenac. Similar observation was reported by Molinari et al. where the measurement of UV absorbance for diclofenac solutions at pH 2 and 6 resulted in an absorbance peak at the same wavelength but at lower intensity in the case of acidic solution [14]. Nonetheless, this behaviour did not cause any problem since diclofenac presented a high extraction for pH range between 4 and 7 for all the extractants used (10 % of each Cy923, TOA, and 20 % of TBP).

As for ibuprofen with a pKa of 4.9, a higher extraction is achieved for

a pH <6. In this range of pH, ibuprofen is mildly undissociated which is less polar and easily removed from the aqueous solution by neutral extractants. In fact, the pH affects the dissociation of the carboxyl group. These results are in accordance with a study by Razo-Lazcano et al. for the removal of ibuprofen with TOA at pH 2 [24]. For instance, the results depicted in Fig. 2 show that at low pH (pH ≤ 4), high IBP extraction is reached, while for pH ≥7, the drug concentration in the organic phase decreases drastically. The results obtained show that around 95 % of extraction was achieved at a pH range between 5 and 6, therefore, a high acidic medium is not required and extreme pH alteration can be avoided. Alternatively, carbamazepine is characterized by two pKa values: 3.9 and 15.9. The measurement of pH at equilibrium indicates that this pharmaceutical was partially extracted with Cy923 and TBP, though TOA was ineffective to extract CBZ at a different range of pH. Consequently, 10 % of Versatic Acid 10 (neodecanoic acid) was tested as a potential extractant for carbamazepine. The purpose was to ensure a back extraction for CBZ when applying SLM. As a result, carbamazepine was poorly extracted at basic pH = 13, the extraction percentage tends to decrease for a pH higher than the pKa value as shown in Fig. 2d. The highest value of extraction was obtained for acidic pH 2 and the lowest percentage was at a pH 14, therefore Versatic Acid 10 was selected for
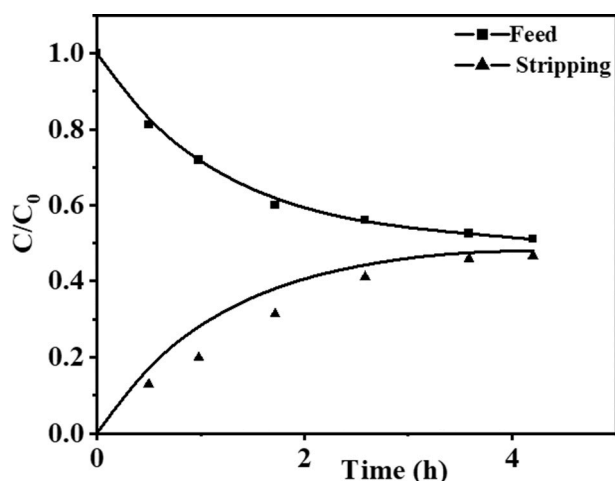
Fig. 3. Evolution CBZ concentration vs time in the feed phase with 10 % Versatic Acid (C_0 = 30 mg/L, pH = 4), and stripping phase (pH stripping = 13.5).

the SLM experiment for the amino-functional group. The extraction of carbamazepine with TOA was studied by Grote et al. [25]. The results obtained confirm the poor extraction of CBZ using TOA (a <5 %). On the other hand, they were able to increase the back extraction of carbamazepine from 8 to 30 % when using Cu(II)-chelate of 2-ethylhexanoic acid as a carrier dissolved in decanol [25].

### 3.2. Transport studies through SLM

Transport through SLM tests were performed for diclofenac, ibuprofen and carbamazepine with each of the following: 10 % (v/v) of Cy923, TOA, and 20 % (v/v) of TBP diluted in kerosene.

Considering the acid-base properties of the pharmaceutical used, diclofenac and ibuprofen contain a carboxylic group in their structure. Hence, their dissociation reaction in aqueous media is the following:

$$HA \leftrightarrow A^- + H^+$$
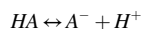
Taking into account that Cy923, TBP, and TOA extract neutral species, the extraction process was carried out at neutral pH 6 and 5 for diclofenac and ibuprofen respectively. Diffusion occurs from the bulk phase of the feed to the inner surface of the membrane. The molecules of the organic carrier (E) can solvate the non-charged form of the drug HA permitting the extraction of this molecule to the organic phase, and the reaction equation for the extraction step is the following:

$$HA + n\,\overleftarrow{E} \rightleftharpoons \overline{E_n \cdot HA}$$
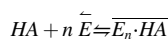
The pharmaceutical organic complex diffuses through the membrane phase due to the concentration gradient to reach the membrane/product interface where the complex is broken by the hydroxide ion present in the receiving phase and the pharmaceutical is released. The reaction occurring in the stripping phase is the following:

$$\overline{E_n \cdot HA} + OH^- \rightleftharpoons n\,\overline{E} + A^- + H_2O$$
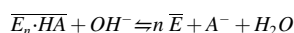
Based on results obtained with liquid-liquid extraction, membrane experiments were carried out using the optimized parameters for initial pH in the feed phase (pH 6 for diclofenac and pH 5 for ibuprofen), drug concentration (30 mg/L). The permeability coefficient for each organic solvent is calculated using Eq. (1) as well as the evaluation of concentration in the feed and the stripping is shown in Fig. 3.

For diclofenac, although the three carriers Cy923, TBP, and TOA were able to extract diclofenac from the feed to the receiving phase, the rate of transport was higher using Cy923. More than 80 % of diclofenac was transported after 3 h using 10 % Cy923 (Fig. 4). The transport was
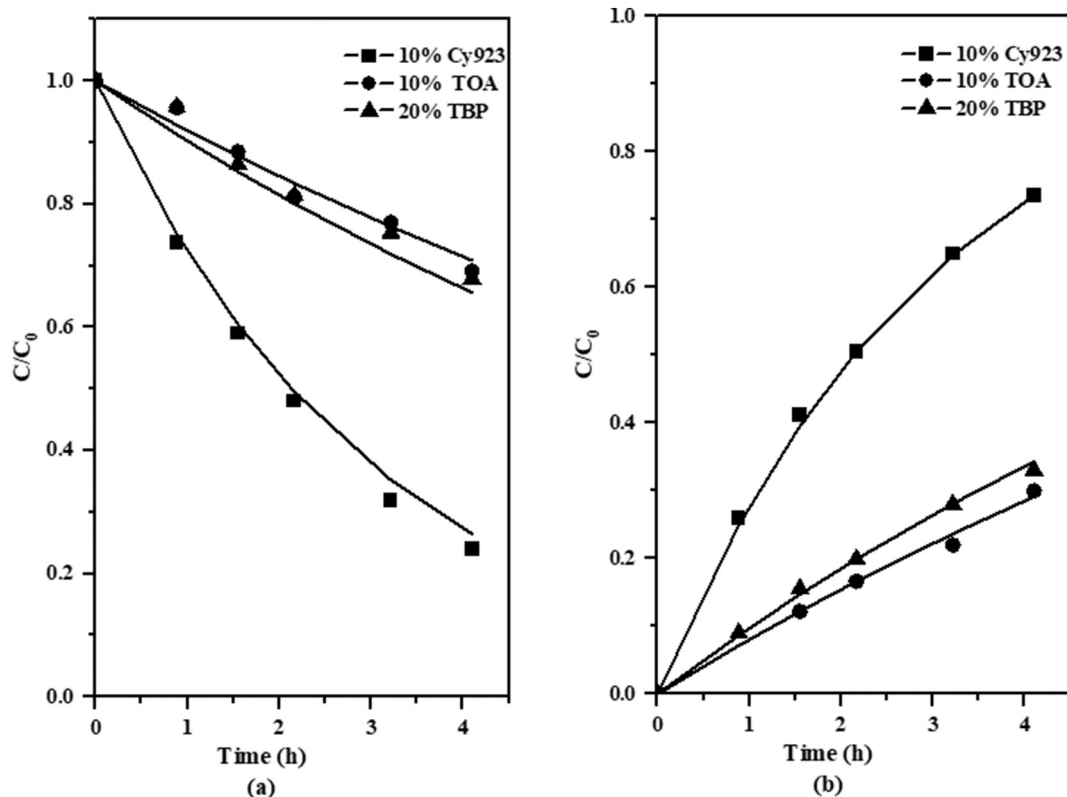

Fig. 4. (a) Evolution of DCF concentration in the feed phase vs time for different extractants (C_0 = 30 mg/L; pH 6.0) and (b) evolution of DCF concentration in the stripping phase vs time with different extractants (pH = 10).
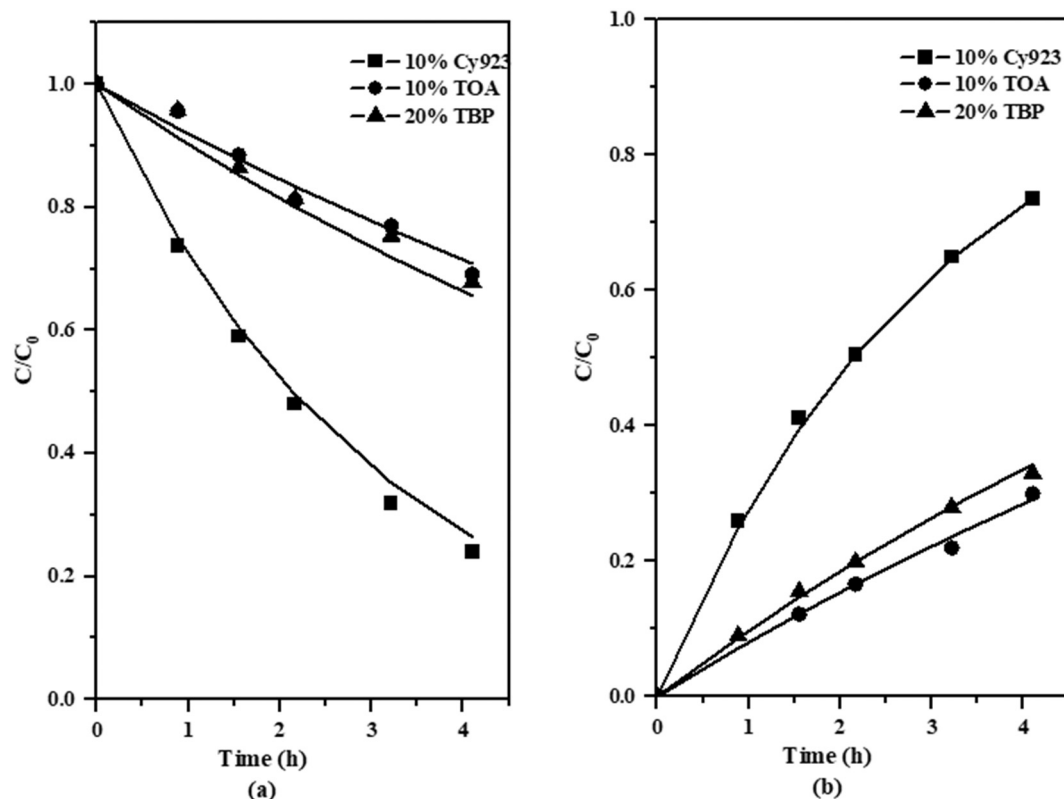
Fig. 5. (a) Evolution of IBP concentration in the feed phase vs time for different extractants ($C_0 = 30$ mg/L; pH = 5.0) and (b) evolution of IBP concentration in the stripping phase vs time with different extractants (pH = 11).

examined by determining the permeability coefficient (P) with all three extractants, and the highest value was 6.3 cm/h with 10 % (v/v) Cy923. The complex formed with Cy923 is transported faster than TBP and TOA complex. Therefore, Cy923 diluted in kerosene was selected to extract diclofenac. Cy923 is considered a cheaper extractant with better stability compared to tributylphosphate [18,26].

For ibuprofen, maintaining the pH gradient between the two phases was a major key for extraction and back extraction with the three organic solvents. During the experiment, the pH in the feed phase increases to a value of 7 as ibuprofen is extracted, thereafter all the experiments were carried out at a pH of approximately 5. The influence of aqueous feed pH for the removal of ibuprofen with hollow fiber membrane was evaluated by Williams et al. [21]. Extraction of ibuprofen increased as the feed pH decreased and the highest removal value (99 %) was observed when the initial pH was set to 2 [21]. Based on Fig. 5, the transfer of the complex formed with Cy923 is faster than the one formed TOA and TBP (P = 6.7 cm/h) confirming the results obtained previously with L-L extraction (Fig. 2c). Less than 2 h was needed for 50 % of the IBP to be transported to the stripping phase. Therefore, Cy923 is selected as the extractant in SLM experiment for ibuprofen.

As for carbamazepine, the transport from the feed phase was tested with 10 % (v/v) Versatic Acid 10 and 1 M of NaOH to ensure a back-extraction in the stripping phase. The permeability coefficient obtained was 8.07 cm/h. The evolution of CBZ concentrations in the feed and stripping cells is shown in Fig. 3. The results of the graph shows that the concentration of carbamazepine decreased gradually compared to other drugs in which 50 % of the drug was transported after 3 h of the experiment.

3.3. Effect of extractant concentration

The influence of Cy923, TOA and TBP concentration in the transport process for DCF and IBP was evaluated. SLM impregnated with a higher
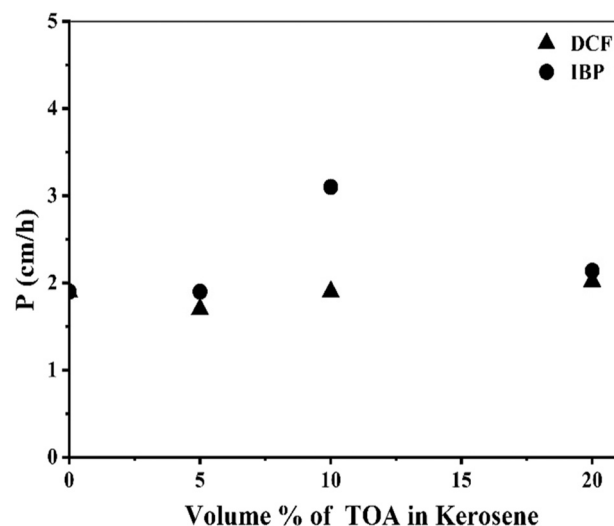

Fig. 6. Effect of TOA concentration on diclofenac and ibuprofen permeability coefficient.

concentration of TOA did not have any effect on the transfer of DCF when varying the extractant concentration from 10 % to 50 % in kerosene (Fig. 6). As for ibuprofen, the transport decrease for a TOA concentration higher than 10 %. This reverse effect is attributed to the increase in viscosity. Therefore, when the concentration of extractant is high, the transport flux decreases due to the higher viscosity of the organic phase [11,27]. In addition, the complex formed with TOA was not easily transported through the membrane compared to the rest of organic used. This effect was pointed out as well by Razo-Lazcano et al. [24] where the stripping efficiency of ibuprofen decreased when
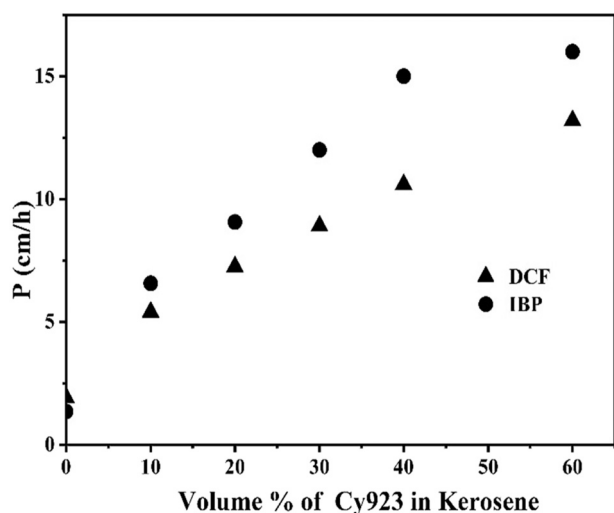
Fig. 7. Effect of CY923 concentration on diclofenac and ibuprofen permeability coefficient.
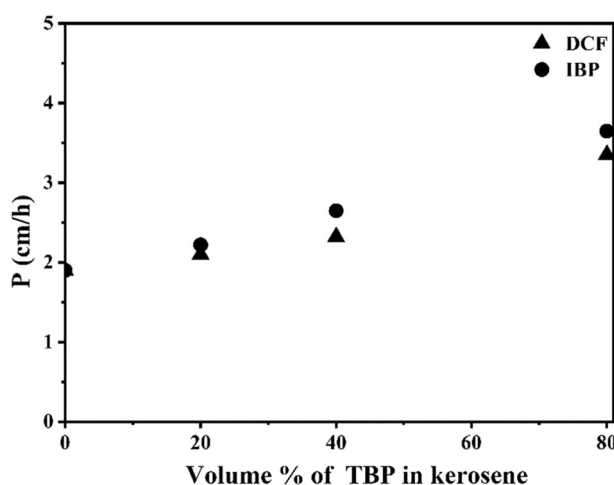

Fig. 8. Effect of TBP concentration on diclofenac and ibuprofen permeability coefficient.

increasing the concentration of TOA from 1 % to 2 %. They required the addition a surfactant to enhance the solute flux [24] to achieve a maximum IBP transfer (98 %) was reached to the stripping phase after 10 h of experiment. Nevertheless, a high operation time can affect the stability and the lifetime of the membrane as the need for a surfactant can increase the cost.

As for Cy923 and TBP, the permeability coefficient increased linearly with the concentration. The dependence of extractant concentration and permeability coefficient are shown in Figs. 7 and 8.

For Cy923, the transport process was controlled by the diffusion with <60 % (v/v) for both drugs The permeability coefficient of DCF and IBP increased with the concentration of Cy923 and the maximum value obtained was with 40 % of Cy923 in kerosene. The analysis of the results indicates that the diffusion coefficient controls the transport process when the concentration of Cy923 is ≤60 % (v/v). Increasing the organic extractant concentration leads to higher viscosity of the organic phase which can reduce the diffusion coefficient due to the effect of the shear stress [27]. Previous studies proved that this complex species formation between the contaminant and the organic extractant does not only depend on the equilibrium constant of the reaction mechanisms, but also on the viscosity effect of the organic extractants which is governed by Stokes-Einstein equation [16,26]. The variation of permeability

coefficient with Cyanex 923 concentration was reported by different studies for the removal of iron(III) [16] cadmium(II) [18], and phenolic compounds [27]. The optimum concentration of Cyanex 923 required for a quantitative extraction, depends on the nature of the feed and stripping phase, temperature and pH [28].

Although the permeability coefficient for IBU and DCF increased with the concentration of TBP (Fig. 8), however the highest value for the permeability coefficient obtained with 80 % of TBP (3.65 cm/h) was relatively lower than the one obtained with 10 % Cyanex 923 (6.3 cm/h) in kerosene. The comparison between these two organic carriers has been conducted by Pavon et al. for the extraction of phenolic compounds (vanillin), they obtained a higher permeability with Cy923 in kerosene [27,28]. An additional experiment was conducted to verify this statement using a PTFE membrane with smaller pore diameters (0.22 μm). In this case, increasing the concentration of Cy923 from 10 % to 40 % (v/v) did not affect the transport of DCF or the permeability coefficient. The appropriate values of viscosity are depending on separation targets, chemicals used, physicochemical properties of the polymeric support, and operating conditions [28]. In this case 40 % of Cy923 was selected.

3.4. Effect of membrane support

As described in the previous section, the polymeric support of the membrane consists of microporous hydrophobic polymers that does not play an active role in the separation but provide structural support for the membrane phase, which is the active component in the separation [11,29]. Two types of polymeric flat sheet supports (PTFE and PVDF) were studied and diclofenac was selected as a case study to investigate the effects. The characteristics of both membranes are mentioned in the previous section. The use of PVDF as support for liquid membrane has been reported by various research studies for the separation, recovery, and extraction of different chemicals [17,18,30].

The membranes were impregnated under the same conditions tested in the transport studies (10 % of Cy923, concentration of DCF in the feed 30 mg/L, and concentration of NaOH in the stripping 0.1 mM). In the case of polyvinylidene fluoride (PVDF), the rate of transport of pharmaceuticals was lower than the one obtained with PTFE membrane, the permeability coefficient determined was 3.9 cm/h <6.3 cm/h In SLM, the diffusion coefficient has to be corrected according to the characteristic of the polymeric membrane used The flux in supported liquid membrane can be calculated through the following equation:

$$J = -D\frac{\Delta Cmi}{\delta} \tag{2}$$

where J is the diffusion molar flux (mol DCF·s⁻¹ m⁻²), D is the diffusion coefficient ($m^2 \cdot s^{-1}$), Cmi, is the concentration of diclofenac at a point between both internal sides of the membrane (mol·L⁻¹) and δ is the membrane thickness (m). Besides, the diffusion coefficient (D) is proportionally related to the porosity of the membrane.

Therefore, it is expected to obtain a higher permeability coefficient with PTFE membrane characterized by higher porosity and smaller thickness compared to PVDF membrane (Table 2). Harruddin et al. compared the performance of three types of polymeric membranes (PES, PSF, and PVDF) with different porosity (48.9, 27.5, and 23.6 %, respectively) for the removal of acetic acid from aqueous solution; they obtained 86 % of removal efficiency after 5 h of experiment with PES membrane with the highest porosity [29].

3.5. Stability of the membrane

Instability of the membrane can occur when the organic extractant fails to be retained inside the membrane pore during the process. SLM membranes present several advantages, such as high selectivity, operational simplicity, low solvent inventory, and low energy consumption however they can fall back on their stability and lifetime [11,31].

Table 4
Permeability coefficient (cm/h) for three consecutive runs.

|	PTFE support	PVDF support
1st run	10.1	5.5
2nd run	5.23	3.4
3rd run	4.1	3.2

For the stability studies, the pores of the microporous support were filled with the organic solution of 40 % Cy923. It is favoured to use organic liquid with high viscosity that exhibits high organic-water interfacial to increase the stability [32]. The stability of both PVDF and PTFE polymer support was tested by conducting transport experiments for diclofenac for three consecutive runs of 3 h and the permeability coefficients determined with Eq. (1) for each run are shown in Table 4.

It is essential to take into account the properties of the polymer material. The PTFE membrane exhibits a rough fibrous structure compared to PVDF membrane with a smoother surface. The comparison between the coefficient of permeability for the first run and the subsequent two for both polymeric support shows that PVDF is more stable after 3 consecutive operations. Although PTFE membranes are characterized by higher porosity yet higher porosity prompts that more pore channels are opened for diffusion which can cause loss of organic solvent [11,32]. Moreover, according to Table 4, the permeability of the membrane shows a variation between the first two runs but maintains a similar value for the following two. To investigate this behaviour, the organic solvent solution was contacted with water for 20 min and then used to impregnate the membrane. The test was conducted with 30 mg/L of diclofenac under the same operating condition as the transport studies with PTFE membrane. The permeability decreased by 60 % (data not shown). The decrease in transport rate after contacting the organic solution with water is attributed to the increase in the viscosity of the organic solvent. Similar results were reported by Batchu et al. [33] who

investigated the extraction of water molecules by Cyanex 923 from aqueous solutions by the Karl Fisher titration method. They found that the co-extraction of water molecules by 1 M Cyanex 923 was 24.6 g/L. This solubility tends to decrease as the concentration of organic solute decreases in water [33].

Different studies have analysed the influence of these factors but many have discarded the importance of the method applied to fill the pores of the polymeric support [34]. To increase the long-term runs of SLM, the pores of the polymeric support PTFE was filled with the organic solution of Cy923 40 % (v/v) in two different ways: under vacuum for 24 h, and at atmospheric pressure but assisted by ultrasounds for 30 min. The results after three consecutive runs are shown in Fig. 9.

The transport of diclofenac for both methods was enhanced from the first run Fig. 9a and b and higher permeability coefficient was obtained. More than 50 % of diclofenac was transported in 3 h after several runs. It was noticed that supported liquid membranes prepared by vacuum method provided better results than the membranes prepared by ultrasound method as seen from the higher values of transport efficiency for the first two runs and a higher flux where almost 90 % of diclofenac was transported after 2 h. Acoustical streaming and cavitation produced when ultrasounds pass through a liquid medium can increase pore filling. A study done by Kyllönen et al. suggested that this enhancement of performance is due to the increase in pore radius and pore density [35]. While proving that ultrasound can enhance the stability of the membrane, it usually adds additional cost to the treatment, thus it is favourable to have the polymeric support in contract with the organic solvent under vacuum to optimize the stability and the transfer of pharmaceuticals through SLM. The instability of SLM remains the main issue for their applications and further studies are recommended to increase their lifetime by studying the influence of the different components of the liquid membrane.
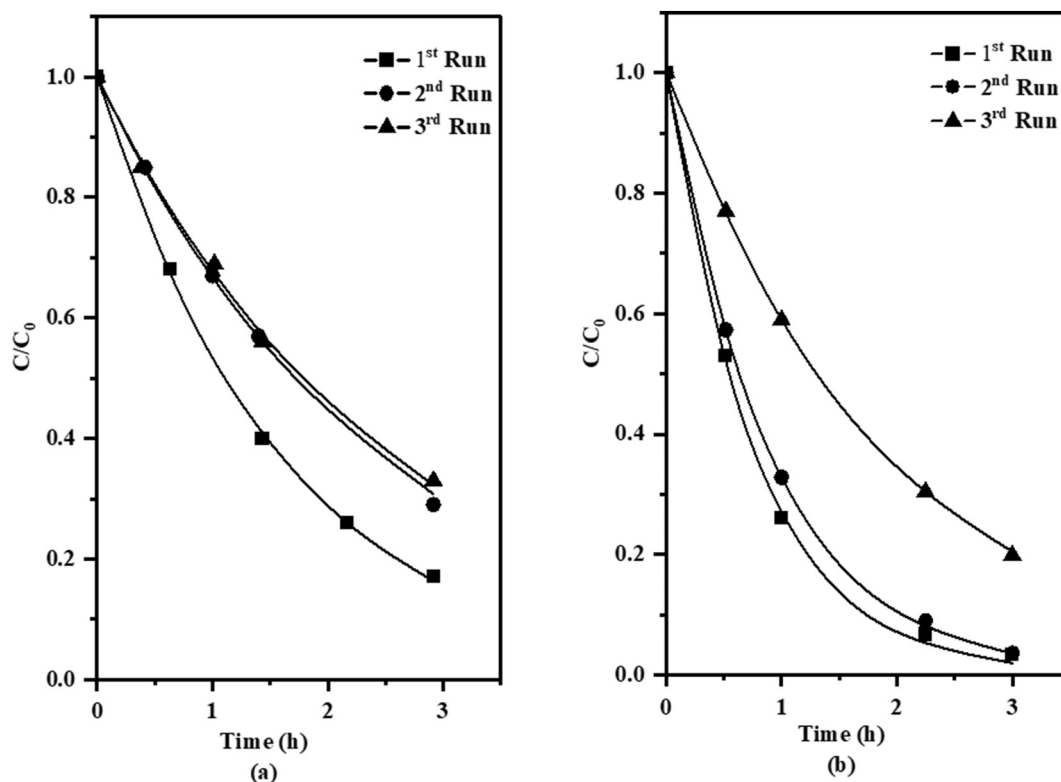
Fig. 9. Evolution of DCF concentration for three consecutive runs. (a) Ultrasound for 30 min at 50 kHz and 40 % Cy923 of organic solvent. (b) PTFE membrane under vacuum for 24 h.

4. Conclusions

The removal of diclofenac, ibuprofen, and carbamazepine from aqueous solutions has been performed with a flat sheet supported liquid membrane. Different organic solvents were tested as possible extractants. Diclofenac and ibuprofen were transported at a faster rate with 10 % of Cy923 and carbamazepine was transported to the stripping phase with 10 % of Versatic Acid 10 diluted in kerosene. Different operating parameters influencing SLM experiments were varied and the performance and the stability of SLM were analysed. It is essential to find the optimum conditions in order to increase the lifetime of the membrane without inhibiting the transport rate.

Particularly in this following study, The integration of SLM in the abatement of persisting pharmaceutical contaminants shows promising results since 98 % of different pharmaceuticals were removed with a minimal amount of organic extractants. The purpose was to investigate SLM in the removal of pharmaceutical contaminants efficiently and effectively. Further studies are recommended to overcome the instability that is associated with these types of membranes and to investigate the possibility of combining this liquid membrane with different established wastewater technologies to achieve high and complete removal of pharmaceuticals at a low footprint.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Mary Farah reports financial support was provided by the Rovira i Virgili University Higher Technical School of Chemical Engineering and by the grant RTI2018-096467-B-I00 funded by MCIN/AEI/10.PK039/501100011033 and "ERDF A way of making Europe". The authors research group is recognized by the Comissionat per a Universitats i Recerca, DIUE de la Generalitat de Catalunya (2017 SGR 396).

Data availability

Data will be made available on request.

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