Effects of membrane fouling on the nanofiltration of pharmaceutically active compounds (PhACs): Mechanisms and role of membrane pore size

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Abstract

The influence of membrane fouling on the retention of pharmaceutically active compounds (PhACs) by three nanofiltration membranes was investigated in this study. Membrane fouling was achieved with a foulant cocktail containing model organic foulant in a background electrolyte solution. The effects of membrane fouling on the separation process was delineated by comparing the retention values of clean and fouled membranes and relate them to the membrane properties as well as physicochemical characteristics of the PhACs. Fouling was more severe for the larger pore size TFC-SR2 and NF 270 membranes as compared to the smaller pore size NF 90 membrane. More importantly, the influence of membrane fouling on the retention of PhACs was found largely dependent upon membrane pore size. It was hypothesised that such influence was governed by three distinctive mechanisms: modification of the membrane charge surface, pore restriction, and cake enhanced concentration polarisation. The presence of the fouling layer could affect the retention behavior of charged solutes by altering the membrane surface charge density. While the role of this surface charge modification mechanism was clear for inorganic salts, it was less obvious for the negatively charged pharmaceutical species examined in this investigation, possibly due to the interference of the pore restriction mechanism. Behavior of the very loose TFC-SR2 membrane was found dominated by pore restriction and this membrane consistently showed an increase in retention under fouled conditions. In contrast, evidence of the cake enhanced concentration polarisation effect was observed with the smaller pore size NF 270 and NF 90 membranes.

Keywords: Nanofiltration; Organic fouling; Pharmaceutically active compounds; Water recycling; Pore size; Pore restriction; Cake enhanced concentration polarisation

1. Introduction

Membrane processes such as nanofiltration (NF) and reverse osmosis (RO) play an important role in the production of high quality reclaimed water where trace organic contaminants are to be removed. Examples of water recycling schemes using NF/RO processes are quite numerous and include a diverse range of water reuse applications such as managed aquifer recharge, municipal dual-reticulation systems, and industrial and agricultural uses [1]. Applications of NF/RO treatment processes for indirect potable water recycling have also been demonstrated in several countries including Singapore, Belgium, and the USA [2,3]. In such schemes, the produced NF/RO filtrate is injected into either a water supply aquifer or reservoir, recaptured after a certain environmental residence time, and repurified in a drinking water production facility [2,3]. The satisfactory elimination of trace organic contaminants is of paramount importance for the protection of public health. In fact, previous studies have demonstrated that organic contaminants such as steroid hormones and pharmaceutically active compounds (PhACs) are ubiquitous in most secondary treated effluent and sewage impacted water bodies at trace level, typically in the range of several micrograms per liter of less [4,5]. In particular, some PhACs such as carbamazepine can be quite persistent to the conventional biological sewage treatment process [5] but can be effectively removed by nanofiltration or reverse osmosis [6–8].

Despite a widespread application of membrane filtration processes including nanofiltration and reverse osmosis in the water industry, the current knowledge base regarding the separation of trace organic contaminants remain limited. In fact, recent review articles have highlighted that the removal mechanisms of trace contaminants are complex and can be governed by many factors such as membrane characteristics, physicochemical properties of the solutes, and solution chemistry [1,9]. Of a particular note, little is known about the effects membrane fouling on the retention of trace organic contaminants. Indeed, membrane
fouling is an inherent phenomenon of full scale water recy-
cling operation using NF/RO membranes due to the presence
of substantial amount of organic macromolecules in secondary
treated effluent. Recent studies have reported that the fouling
layer can considerably alter the separation behaviour of trace
contaminants, resulting in either an increase or a decrease in
retention as compared to a clean membrane (or no fouling) condition [10–12]. More importantly, such studies also highlighted
the need for more research to elucidate the underlying mech-
nisms, by which membrane fouling affect the retention of trace
contaminants by NF/RO membranes.

This study aimed to elucidate the effects of membrane foul-
ing on the retention of pharmaceutically active compounds by
three commercially available NF membranes. Experiments were
conducted with three pharmaceuticals – namely sulfamethoxa-
zole, ibuprofen, and carbamazepine – representing the emerging
trace organic contaminants commonly encountered in secondary
treated effluent and sewage impacted water bodies using a cross-
flow NF/RO membrane filtration test unit. Membrane fouling
was induced by a foulant cocktail containing organic matter in a
background electrolyte solution. The effects of membrane foul-
ing on the retention of the PhACs were examined with respect to
the membrane pore sizes, speciation of the compounds, and the
membrane fouling behaviours. Mechanisms possibly account-
able for the effects of membrane fouling on trace contaminant
retention were then proposed and delineated.

2. Materials and methods

2.1. Nanofiltration membranes

Three nanofiltration (NF) membranes – denoted NF 90, NF
270, and TFC-SR2 – were used in this investigation. The first
two membranes were supplied by Dow FilmTec (Minneapolis,
MN) and the last one was supplied by Koch Membrane Systems
(San Diego, CA). According to the manufacturers, these mem-
branes are polyamide thin-film composite with a microporous
polysulfone supporting layer. The membranes were received as
flat sheet samples and were stored dry at 4°C.

2.2. Chemicals and reagents

Sigma–Aldrich humic acid (St. Louis, MO) was selected as
a model organic foulant in this study because it is readily avail-
able and has been quite well characterized. This Aldrich humic
acid has been previously used in numerous membrane fouling
investigations [13–19]. Humic acid (HA) is a major component
of natural organic matter that can be found in soil, natural waters
as well as wastewater. It contains a complex and heterogeneous
group of many humic molecules, which can be described as a
supramolecular colloidal mixture [20]. Their molecular weights
are typically above 50,000 Da [21]. The recorded elementary
composition of the Sigma–Aldrich humic acid in the literature
is 60% C, 4.47% H, 34.5% O, and 0.96% N [22]. The car-
boxylic acidity of this humic acid is 3.4 mequiv./g [21]. All
other chemicals and reagents used in this study were of analy-
tical grade. Sodium chloride, calcium chloride, and sodium
bicarbonate were used to prepare the background electrolytes.
Adjustment of the feed water pH was carried out with sodium
hydroxide (1 M) or hydrochloric acid (1 M).

Three common pharmaceuticals – sulfamethoxazole, carba-
mazepine, and ibuprofen – were selected for this study. Their
intrinsic physicochemical properties together with molecular
structures are presented in Table 1. These pharmaceuticals are
some of the most common occurring trace contaminants in sec-
tened effluent and sewage impacted water bodies. They
represent three different drug categories: sulfamethoxazole is
one of the most frequently used antibiotics; carbamazepine is
a widely used anti-epileptic drug; and ibuprofen is a common
anti-inflammatory agent. The compounds were purchased from
Sigma–Aldrich (St. Louis, MO). The purity of these chemicals
was reported to be 99% or higher. The pharmaceuticals were
first dissolved in pure methanol to make up stock solutions of
1 g/L. The stock solutions were stored at <4°C and were used
within 1 month.

2.3. Crossflow membrane filtration system

A laboratory-scale, crossflow membrane filtration test unit
with a rectangular stainless steel crossflow cell was used in

![Table 1: Intrinsic physicochemical properties of pharmaceuticals](https://example.com/table1.png)

this study. This cell has an effective membrane area of 40 cm² (4 cm × 10 cm) with a channel height of 2 mm. The unit utilises a Hydra-Cell pump (Wanner Engineering Inc., Minneapolis, MN) capable of providing pressures up to 6800 kPa and a flow rate of 4.2 l/min. The temperature of the test solution was kept constant using a chiller/heater (Neslab RTE 7) equipped with a stainless steel heat exchanger coil, which was submerged directly into a stainless steel reservoir. Permeate flow was measured by a digital flow meter (Optiflow 1000, Agilent Technologies, Palo Alto, CA) connected to a PC, and the crossflow rate was monitored with a rotameter.

2.4. Experimental protocol

The fouling and subsequent retention experimental protocol was conducted in three steps: compacting, fouling development, and retention test, as schematically shown in Fig. 1. First, the membrane was compacted using deionised water at 1800 kPa for at least 1 h until a stable baseline flux has been obtained. Fouling layer was then allowed to develop using a foulant cocktail consisting of a specified amount of humic acid in a background electrolyte solution containing 20 mM NaCl, 1 mM NaHCO₃, and 1 mM CaCl₂. Volume of the feed water solution was kept constant at 20 L. Temperature of the experimental system was equilibrated for 1 h. Temperature of the experimental solution was kept constant at 20 ± 0.1 °C. Both permeate and retentate were recirculated back to the feed reservoir throughout the entire experiment. To examine PhAC retention by the clean membranes, a similar protocol but without the fouling development step was adapted. Observed retention is defined as \( R = \frac{100 \times (1 - C_P/C_F)}{C_F} \), where \( C_P \) and \( C_F \) are the permeate and feed concentrations, respectively.

2.5. Analytical methods

A Shimadzu HPLC system (Shimadzu, Kyoto, Japan) equipped with a Supelco Drug Discovery C-18 column (with diameter, length and pore size of 4.6 mm, 150 mm and 5 μm, respectively) and UV–vis detector was used to measure the pharmaceutical concentrations in the feed and permeate. The detection wavelength was set at 280 nm for sulfamethoxazole and carbamazepine, and 225 nm for ibuprofen. The mobile phase used for gradient elution was milliQ grade deionised water buffered with 0.0025 M KH₂PO₄ and acetonitrile, which was delivered at 1 mL/min through the column. A sample injection volume of 50 μL was used. Calibration yielded standard curves with coefficients of determination (\( R^2 \)) greater than 0.99 within the range of experimental concentrations used. The analysis was carried out immediately on the conclusion of each experiment.

3. Results and discussion

3.1. Membrane characteristics

All three nanofiltration membranes selected for this study consist of a very thin polyamide active layer, which determines the membrane separation properties. Although these layers are similar in composition, the exact polymeric make-ups are unknown and thought to be quite different. Consequently, these membranes differ considerably from one another in their characteristics (Table 2). Their pore sizes have been previously characterized by challenging the membranes with a series of inert organic tracers of various molecular weights and applying a pore transport model [23,24]. They represent a wide range of membrane pore size in the order of increasing pore size as follows: NF 90 < NF 270 < TFC-SR2. This is also reflected by their

Table 2
Properties of the membranes used in this study

<table>
<thead>
<tr>
<th>Membrane</th>
<th>Pure water permeability (L m⁻² h⁻¹ bar⁻¹)</th>
<th>Average pore diameter (nm)</th>
<th>NaCl retention (%)</th>
<th>Virgin membrane zeta potential (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>pH 4</td>
</tr>
<tr>
<td>NF 90</td>
<td>6.4</td>
<td>0.68</td>
<td>85.0</td>
<td>5.1</td>
</tr>
<tr>
<td>NF 270</td>
<td>13.5</td>
<td>0.84</td>
<td>40.0</td>
<td>-8.0</td>
</tr>
<tr>
<td>TFC-SR2</td>
<td>15.4</td>
<td>1.28</td>
<td>9.8</td>
<td>-4.7</td>
</tr>
</tbody>
</table>

* Ref. [24].
pure water permeate flux (Table 2). The NF 90 is a relatively tight NF membrane with an average pore diameter of only 0.68 nm. In contrast, the NF 270 can be considered as a loose NF membrane and the TFC-SR2 is a very loose NF membrane with average pore diameters of 0.84 and 1.28 nm, respectively. Indeed, the average pore size of the TFC-SR2 membrane is comparatively larger than the dimensions of the three pharmaceuticals examined in this investigation (see Table 1). Because the polyamide layer that makes up the membrane active layer contains both carboxylic and amine functional groups that can ionize in an aqueous solution [25,26], the membrane surface zeta potential can vary as the solution pH decreases or increases. All three membranes are negatively charged at high pH and they become more negative as the solution pH increases. Of a particular note, at high pH (above pH 6) the NF 90 and NF 270 appear to be more negative than the TFC-SR2. This together with the fact that TFC-SR2 is a very loose NF membrane can explain a very low sodium chloride retention value by this membrane as can be seen in Table 2.

3.2. Physicochemical properties of the selected PhACs

The three pharmaceuticals selected for this study have both similarly associating and distinguishing features. Molecular weights of these compounds lie in a relatively narrow range (see Table 1), which makes them ideal for the comparison and examination of the steric and electrostatic removal mechanisms by the chosen membranes. The compounds differ greatly in several parameters, particularly in their speciation behavior, solubility in water, and hydrophobicity. While carbamazepine is uncharged at common pH conditions typical of natural water or wastewater, both ibuprofen and sulfamethoxazole exhibit a wide variation in speciation (or charge) and physicochemical properties. At pH below its pKₐ value (pH 4.4), ibuprofen exists as a neutral species. Above this pKₐ value, ibuprofen attains a negative charge. Sulfamethoxazole has two ionisable amine groups. As a result, in an aqueous solution, sulfamethoxazole can exist in positive, neutral, as well as negative forms. At pH in between the compound’s pKₐ values (pH 1.4 and 5.8), sulfamethoxazole exists predominantly as a neutral species while above the compound’s second pKₐ value (pH 5.8), it becomes a negatively charged species [6]. The solubility and hydrophobicity of these three compounds mirror closely their speciation as a function of pH (Fig. 2). Both sulfamethoxazole and ibuprofen are highly soluble at pH value in the alkaline region where the compounds are negatively charged. Their solubility decreases sharply as the solution pH decreases. In contrast, the solubility of carbamazepine is not affected by the solution pH. Similar observation can be made for the effective hydrophobicity of these compounds (log D), which measure their adsorptive affinity toward the membranes. While ibuprofen is quite hydrophobic at less than pH 5, the hydrophobicity of this compound decreases significantly as the solution pH increases. On the other hand, both sulfamethoxazole and carbamazepine are relatively hydrophilic at all pH in the range between pH 4 and 10. This suggests that hydrophobic adsorption of these compounds to the membranes in the pH range of natural waters can be negligible. Furthermore, variations in charge and other physicochemical properties as a function of pH may have important implications for the separation mechanisms of these pharmaceuticals.

3.3. Fouling behavior

Membrane fouling is governed by the interplay between chemical and physical (hydrodynamic) interactions [21,27]. Previous studies have shown that organic fouling was most severe at low pH, high ionic strength, and particularly with the presence of calcium ions [16,18,19,21,28–30]. These effects, which were induced by the feed solution chemistries, on membrane fouling were explained by the interactions between the rather hydrophobic humic acid foulant and the fouled membrane surface [29,30]. Due to the protonation of the carboxylic and phenolic groups, which are prevalent in humic acids, a decrease in pH could result in a lower charge density of these organics. Similarly, high ionic strength compresses the electric double layer, neutralises, and screens the charge of the humic acid molecules. Both phenomena lessen the electrostatic repulsion forces between humic acid molecules in bulk solution and those already deposited on the membrane surface, leading to an increase in foulant-fouled membrane adhesion [29,30]. However, the presence of calcium ions appears to cause a more significant increase in organic fouling [18,29,30]. This is due in part to a more effective charge
neutralization capacity of the divalent calcium ions, but a major reason has been attributed to its unique intermolecular bridging ability that cross-links the organic foulants with one another and with the membrane surface. In fact, the role of calcium in facilitating organic fouling has been systematically illustrated in recent studies, which showed much more severe organic fouling when organic matter was present in the feed water together with 1 mM Ca\(^{2+}\) [29,30].

Fig. 3 shows the normalised permeate flux of the NF 270 membrane during fouling development. The feed water contained varied humic acid concentration in the range from 0 to 40 mg/L in a background electrolyte solution. While there was no fouling in the absence of the organic foulants, severe membrane fouling could be observed when the feed solution contained a mixture of humic acids and calcium ions (Fig. 3). The formation of a fouling layer was confirmed by visual observation at the end of each experiment, which showed a dark brown layer of organic materials firmly attached to the membrane surface. The extent of fouling correlated well with the concentration of humic acid in the feed solution, indicated by the corresponding flux decline in Fig. 3. However, it is interesting to note that increasing the humic acid concentration beyond 20 mg/L did not discernibly increase the rate of fouling or the overall flux decline. Furthermore, a sharp drop in permeate flux was observed within the first 6 h of filtration at all humic acid concentrations (Fig. 3). This was possibly caused by pore restriction and initial deposition of the foulants on the membrane surface. Similar rapid flux decline as a result of initial pore restriction and compound adsorption on the membrane surface have also been reported in a previous study by Van der Bruggen and Vandecasteele [31]. After 6 h of filtration, the flux decline was more gradual. Possibly due to the thickening as well as the compaction of the fouling layer, a near-linear flux decline could be observed at this stage, which lasted for about 12 h. As can be seen in Fig. 3, separate plots of flux decline at this stage for the varying humic acids are essentially parallel. Under the conditions of this investigation, membrane fouling was almost fully developed after approximately 18 h.

Fouling profiles of all three NF membranes following the filtration of a solution containing 20 mg/L humic acid are shown in Fig. 4. Flux decline was consistent for the three repetitive experimental runs for each membrane, indicating an excellent reproducibility. More importantly, a clear correlation between the extent of fouling occurring and the membrane pore size could be observed. Flux decline was more severe for the loose nanofiltration TFC-SR2 and NF 270 membranes as compared to the tighter NF 90 membrane. The corresponding flux declines at the end of the 18 h fouling development stage were 73%, 70%, and 50% for the TFC-SR2, NF 270 and NF 90 membranes, respectively. Similar results were reported by Yuan and Zydney [17,18] and Tang et al. [14] who studied the fouling of MF/UF
and NF/RO osmosis membranes, respectively, using the same Aldrich humic acid as a model organic foulant. In the latter study, the authors attributed this to the greater initial flux of the more permeable membranes rather than the applied pressure [14]. However, because a similar initial flux was used in this study, the phenomena reported here could also be attributed to the greater effect of adsorption and pore restriction (or pore plugging) on the larger pore size membranes. In fact, pore restriction has been reported to be a predominant fouling mechanism of the more porous membranes such as MF and UF [17,18]. Pore restriction was also expected to provide an additional sieving effect that might enhance the separation efficiency of the more porous membranes. This will be discussed further in a later section.

3.4. Fouling effects on inorganic salt retention

The effects of fouling on the membrane separation efficiency were examined by comparing the retention value of clean and fouled membranes. Fig. 5 shows salt retention (estimated by conductivity measurements) as a function of pH by both clean and fouled NF 270 membrane. The fouled NF 270 membranes were previously subjected to various humic acid concentrations to simulate a range of fouling extent. Overall, the results indicate decreased salt retention alongside a lowering of pH, which is consistent for both clean and fouled conditions. However, at high pH, salt retention by the clean (virgin) NF 270 membrane was significantly higher than that by the fouled membrane.

Separation in a nanofiltration process can be governed by steric hindrance (or size exclusion) and electrostatic interactions. Both of these separation mechanisms can be considerably affected by membrane fouling. The presence of a fouling layer can modify the physicochemical characteristics of the membrane surface. Furthermore, pore restriction (or pore plugging) can also result in an additional sieving effect. As the solution pH decreased, surface zeta potential of the virgin (clean) NF 270 membrane decreased sharply (see Table 2). Consequently, electrostatic interaction between ionic species and the membrane surface diminished resulting in a dramatic drop in conductivity retention by the clean NF 270 membrane from 70% at pH 9.5 to only 15% at pH 3.5. In contrast, conductivity retention by the fouled NF 270 membrane at high pH was considerably low and a much more gradual reduction in retention was observed as the solution pH decreased from pH 9.5 to 3.5. This was consistent with the results reported by Tang et al. [13], who showed an almost no variation in zeta potential of the NF 270 membrane fouled with Aldrich humic acid when the solution pH varied in the range between pH 9.5 and 3.5. More importantly, they also revealed that the fouled NF 270 membrane became considerably less negative in the presence of 1 mM of Ca\textsuperscript{2+} [13]. At pH 5 and lower, because charge density of the membrane has been reduced to almost zero, salt retention by the NF 270 membrane was dominated by size exclusion resulting in a slightly higher salt retention by the fouled membranes due to the additional sieving effect caused by the fouling layer. Although the difference in this case was rather marginal, this enhanced retention effect can be better illustrated by examining the larger pore size TFC-SR2 membrane.

Fig. 6 shows a clear improved salt retention by a fouled TFC-SR2 membrane as compared to a virgin one. As discussed previously, this is a very loose NF membrane with rather low surface charge density, indicated by considerably less negative zeta potential when compared to the NF 270 or NF 90 membrane (see Table 2). In addition the two effects discussed above, solute retention behavior can also be influenced by the so-called cake enhanced concentration polarisation, a phenomenon first reported by Elimelech and co-workers [32–34], whereby the fouling cake layer hinders back diffusion of solutes from the membrane surface to the bulk solution. The buildup of solutes at the membrane surface results in a higher solute concentration gradient across the membrane and, thus, a greater solute transport through the membrane and a lower observed solute rejection. This phenomenon is also evident here in this study with the tight NF 90 membrane. Salt retention by a fouled NF 90 membrane was consistently lower than that by a virgin one at all pH (Fig. 6). The NF 90 membrane had a considerably high salt retention and thus could exhibit a prominent concentration polarisation effect. It is noted that the NF 270 membrane might...
also show some cake enhance concentration polarisation effect. This phenomenon is expected to be absent for the very loose TFC-SR2 membrane as this membrane would cause negligible concentration polarisation.

3.5. Fouling effects on pharmaceutical retention

Unlike inorganic salts, physicochemical properties of the pharmaceuticals can vary greatly depending on the solution pH. Such variation can also significantly affect their retention behaviors. Fig. 7 shows the retention of sulfamethoxazole under clean and fouled conditions over the measured pH range. The retention of sulfamethoxazole by both virgin and fouled membranes for each membrane type was pH dependent and significant differences in retention were obtained for the three different membranes tested. High retention by the clean and fouled NF 90 membranes could be seen as the result of predominant size exclusion, though contribution of electrostatic repulsion was also evident by a small decrease in retention when the solution pH dropped below pH 7 as sulfamethoxazole transformed toward a neutral form. The role of electrostatic repulsion as a major retention mechanism of negatively charged organic solutes was more obvious for the NF 270 and TFC-SR2 membranes. The NF 270 membrane also achieved high retention of sulfamethoxazole (almost complete retention) at pH above 8 for a virgin (clean) membrane, with slightly lower retention obtained for a fouled membrane sample. Significantly lower sulfamethoxazole retention values at lower pH, however, were obtained for both clean and fouled membrane samples. Similar retention behaviors were also observed for the TFC-SR2 membrane, although sulfamethoxazole retention by this membrane under both clean and fouled conditions was considerably low.

It is interesting to note the difference in retention behavior under clean and fouled conditions. It is possible that membrane pore size plays an important role in governing such behavior. While the NF 90 membrane showed a small loss in sulfamethoxazole retention at low pH under fouled conditions, retention of sulfamethoxazole by the TFC-SR2 membrane improved under fouled conditions. The observed increase in retention for the TFC-SR2 membrane, which has the largest pore size (average pore diameter of 1.28 nm), can be attributed to pore restriction and possible deposition of organic matter on the pore walls. This fouling on and within the pores of the TFC-SR2 membrane is proposed to result in a reduced porosity and area available for the passage of pharmaceutical molecules. The NF 270 membrane exhibited mixed results, with lower retention observed for the fouled membrane at high pH, while higher retention was observed at the mid-pH range.

The retention of ibuprofen also varied with membrane type, with different behaviors exhibited for the three membranes tested, as can be seen in Fig. 8. The NF 90 membrane showed complete retention under clean membrane conditions, with a slight decrease in retention under fouled conditions around pH 5. This is due to the small pore size of the NF 90 membrane providing almost complete retention of the larger ibuprofen molecule. Due to the speciation of ibuprofen as a function of pH, the retention of this compound by the NF 270 and TFC-SR2 membranes under both clean and fouled conditions was pH dependent. Ibuprofen again showed remarkably high retention at high pH, with decreasing retention occurring for both a clean and fouled membrane sample as the pH was lowered.

Retention of ibuprofen by the NF 90 membrane appears to be largely governed by steric exclusion given the smaller pore size of this membrane compared to the ibuprofen molecule, though there appears to be some contribution to retention from Donnan exclusion (or electrostatic interactions), attributed to a slight decrease in retention around pH 5. This due to the speciation of ibuprofen, which exists primarily as a neutral species at pH below its pKa value (pH 4.4). It is noteworthy that in the absence of electrostatic repulsion, hydrophobic interaction between ibuprofen and the membrane surface become more prominent, resulting in improved retention due to adsorption, which can be seen for both the clean and fouled TFC-SR2 membrane samples. The influence of electrostatic interaction as a
Results reported here indicate that organic fouling can induce considerable effects on the retention of PhACs by NF membranes. However, under both clean and fouled conditions, physicochemical properties of the solutes were found to be major factors governing the separation process. The extent of membrane fouling correlated well with the membrane pore size, with the smaller pore size NF 270 and NF 90 membranes exhibiting the least fouling. More importantly, the influence of membrane fouling on the retention of PhACs was also membrane pore size dependent. Such influence was probably governed by three distinctive mechanisms: modification of the membrane charge surface, pore restriction, and cake enhanced concentration polarisation. The presence of the fouling layer could affect the retention behavior of charged solutes by altering the membrane surface charge density. While the role of this mechanism was clear for inorganic salts, it was less obvious for the negatively charged pharmaceutical species examined in this investigation, possibly due to the interference of the pore restriction mechanism. In fact, behavior of the very loose TFC-SR2 membrane was dominated by pore restriction and this membrane consistently showed an increase in retention under fouled conditions. In contrast, evidence of the cake enhanced concentration polarisation effect could be seen with the smaller pore size NF 270 and NF 90 membranes. It was also observed that magnitude of the influence of membrane fouling on retention, either positive or negative, decreased as the membrane pore size decreased.

4. Conclusion

As can be seen in Table 3, pore restriction is prevalent for the large pore size membrane TFC-SR2 and can lead to a considerable improvement in retention. On the other hand, cake enhanced polarisation concentration can cause a small but nevertheless apparent decrease in pharmaceutical retention by the smaller pore size NF 270 and NF 90 membranes. In addition, the impact of membrane fouling, either positive or negative, decreases in magnitude as the membrane pore size decreases. This is consistent with a previous study which showed that membrane fouling was less important for reverse osmosis membranes with respect to the removal of trace organic contaminants [11].

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Changes in retention of the pharmaceuticals due to membrane fouling</th>
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</thead>
<tbody>
<tr>
<td>TFC-SR2</td>
<td>pH 6</td>
</tr>
<tr>
<td>Sulfamethoxazole</td>
<td>+37</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>+28</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>+19</td>
</tr>
</tbody>
</table>

Positive sign indicates an increase and negative sign indicates a decrease in retention by fouled membranes compared to clean ones (experimental conditions are as in captions of Figs. 7–9).

3.6. Role of membrane pore size

Results reported in this study suggest that organic fouling can influence the retention of pharmaceuticals via three distinctive mechanisms, namely modification of the membrane surface charge, pore restriction, and cake enhanced polarisation concentration effect. These mechanisms can act against one another, which perhaps explains the inconsistency in the literature about the effects of membrane fouling on the removal efficiency of trace organic contaminants. While retention can be improved by pore restriction, cake enhanced polarisation concentration can induce a lower retention. The presence of the fouling layer can also render the membrane surface charge to be more or less negative, hence improving or lessening retention of the charged pharmaceutical species. Contributions of these mechanisms are strongly dependent on the membrane pore size. As can be seen in Table 3, pore restriction is prevalent for the large pore size membrane TFC-SR2 and can lead to a considerable improvement in retention. On the other hand, cake enhanced polarisation concentration can cause a small but nevertheless apparent decrease in pharmaceutical retention by the smaller pore size NF 270 and NF 90 membranes. In addition, the impact of membrane fouling, either positive or negative, decreases in magnitude as the membrane pore size decreases. This is consistent with a previous study which showed that membrane fouling was less important for reverse osmosis membranes with respect to the removal of trace organic contaminants [11].
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