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Nanofiltration removal of pharmaceutically active compounds

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ABSTRACT

Capability of nanofiltration membranes (NF) to remove pharmaceutical active compounds from wastewater streams was investigated. Sulfamethoxazole, diclofenac sodium, hydrochlorothiazide, 4-acetamidoantipyrine, nicotine and ranitinide hydrochloride were selected as model compounds since they are widely produced as pharmaceutical agents. Two commercially available polyamide nanofiltration membranes (NF-90 and NF-270 from Dow FilmTec) were tested. Solute retention by NF-90 membrane was very high in all cases (over 95%), whereas NF-270 retention systematically appeared lower ranging from 75% (nicotine) to 95% (ranitidine hydrochloride). Temporal evolution of flux decline was also investigated. The influence of physicochemical properties of both membrane and solutes on membrane performance was analyzed to explore the main solute-membrane interactions that determine the solute transfer across the membrane. The influence of operation pressure on NF-90 and NF-270 rejection was also studied.

Keywords: Nanofiltration; Pharmaceutical; Water treatment; Sulfamethoxazole; Diclofenac; Hydrochlorothiazide; 4-Acetamidoautipyrine; Nictoine; Ranitidine

1. Introduction

Removal of pharmaceutically active compounds (PhACs) from household pharmaceuticals disposal was classified as an important environmental issue (human health risk) due to their presence in aquatic environment. PhACs are continuously released to the environment often from their original source via domestic wastewater effluent, but also as partially metabolized forms via partial assimilation of them by humans and animals during therapeutic treatments. Different classes of pharmaceuticals such as antibiotics, analgesics, antiepileptic drugs, anti-rheumatics, beta blockers, chemotherapeutics and steroid hormones have been detected from domestic effluents and water reuse plants within the concentration range of micrograms per litre [1,2]. Since most of the detected PhACs in the aquatic environment exhibit a low biological degradability, they could not be completely removed by means of conventional wastewater treatments. Reported removal rates of pharmaceuticals in existing sewage treatment plants are, in general, approximately 40%–60% [3,4]. For this reason, it is crucial to improve the current technologies used in the wastewater treatment plants for elimination of stable refractory pharmaceuticals residues before entering into the aquatic environment.

In the last decade, membrane technology has been proposed as an attractive option for removal a wide variety of organic contaminants, including PhACs, from water [5–9]. Pressure-driven membrane processes,

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notably reverse osmosis (RO) and nanofiltration (NF), are considered feasible and potential methods of organic micropollutants removal from water in terms of solute rejection [10–14]. In particular, numerous studies have attempted to focus on the main transport mechanisms of PhACs through NF/RO commercially available membranes [15–17]. Rejection of pharmaceuticals by these membranes is really complex as consequence of the great number of variables involved in the separation mechanisms. It is influenced by the physicochemical properties of the solute (molecular weight, charge, hydrophobicity), the membrane characteristics (surface hydrohobicity, surface charge, pore size), the solution chemistry (ionic environment, pH, and concentration) and the operational conditions (pressure, permeation rate, cross-flow velocity).

The aim of this work is to explore the role of steric and electrostatic interactions in the removal of pharmaceuticals by two commercial NF membranes (NF-90 and NF-270, DOW FilmTec). The influence on permeate flux and solute rejection of the physicochemical properties of pharmaceuticals and membranes as well as the effect of the solution chemistry and transmembrane pressure on the membrane performance have been analyzed in this article.

2. Materials and methods

The synthetic feed solutions used in experiments were made by dissolving the appropriate chemicals in particle-free, Milli-Q water. The concentration of the feed organic solution was approximately 10 mg l^{-1} for each pharmaceutical compound and the resulting solution pH value was around 7.

2.1. Solutes and membranes

Sulfamethoxazole (SMX), diclofenac sodium (DCF), hydrochlorothiazide (HCT), 4-acetamidoantipyrine (4AAA), nicotine (NCT) and ranitidine hydrochloride (RNT) were selected as pharmaceutical agents and obtained in a pure form from Fluka (SMX, NCT), Alfa Aesar (4AAA), and Sigma-Aldrich (DCF, HCT, RNT). Table 1 summarizes some physicochemical characteristics of these emerging pollutants, such as the logarithm of *n*-octanol/water partition coefficient, $\log K_{OW}$, and the first acid constant, pK_a.

Two nanofiltration membranes, NF-90 and NF-270, supplied by Dow FilmTec were evaluated in this investigation. According to the manufacturers, both membranes are polyamide thin-film composite with a microporous polysulphone supporting layer. NF-270, with a thin active layer made from piperazine and benzenetricarbonyl trichloride, is a typical nanofiltration membrane with applications in the drinking water production. The specifications of the other nanofiltration membrane, NF-90, indicate that it can achieve a high removal of divalent salts and organic compounds from feed water. These two membranes were selected on the basis of their distinctive characteristics, such as surface roughness, molecular weight cut-off (MWCO), zeta-potential value at neutral pH, and hydrophobicity. Both membranes were received as flat sheet samples and stored dry. Table 2 summarizes the most relevant characteristics as given by the membrane manufacturers.

2.2. Membrane filtration protocol

The membranes were tested as flat sheet membrane specimens in a commercial SEPA II cross-flow filtration test cell (Osmonics, Minnetonka, MN). The effective membrane area in the test unit was 139 cm^2. Fig. 1 shows a schematic diagram of the filtration system used in this investigation. The storage tank contained 10 l of organic solution. The experiments designed to study the membrane temporal evolution and pressure influence on membrane rejection were operated in a recycle mode in which all concentrate and permeate streams were flowed back to the feed vessel.

Table 1
Intrinsic characteristics of the selected pharmaceuticals

Compound	Formula	MW(g mol^{-1})	$\log K_{ow}$	pK_a
Sulfamethoxazole (SMX)	$C_{10}H_{11}N_3O_3S$	253.3	0.9	5.8
Diclofenac sodium (DCF)	$C_{14}H_{11}Cl_2NO_2$[1]	296.2[1]	4.5[1]	4.1[1]
Hydrochlorothiazide (HCT)	$C_7H_8ClN_3O_4S_2$	297.7	−0.5	7.9
4-Acetamidoantipyrine (4AAA)	$C_{13}H_{15}N_3O_2$	245.3	−0.1	4.6[2]
Nicotine (NCT)	$C_{10}H_{14}N_2$	162.2	1.1	3.1[2]
Ranitidine hydrochloride (RNT)	$C_{13}H_{22}N_4O_3S \cdot HCl$	350.9	1.3	8.2[2]

[1]Reported values correspond to diclofenac (acid form).
[2]pK_a of the monoprotonated form.

Table 2
Membrane characteristics

	NF-270	NF-90
Manufacturer	Dow/FilmTec	Dow/FilmTec
Classified as	NF	NF
Material (active layer)	Polyamide	Polyamide
MWCO (Da)	300	200
NaCl rejection (%)	40–60	90
Test pressure (psi)	70	70
pH range	3–10	4–11
Membrane charge (pH 7)	Negative	Negative
Contact angle (°)	29.0	63.2

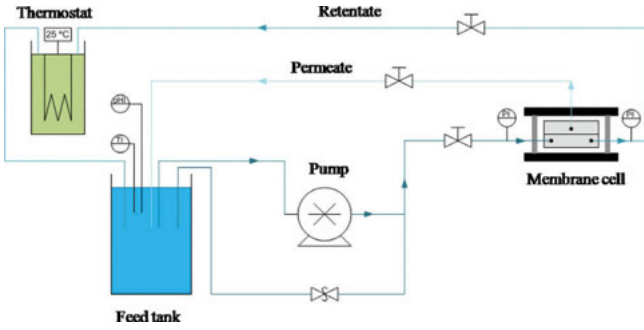

Fig. 1. Schematic diagram of the filtration unit.

Fresh membranes were first soaked in distilled water for approximately 24 h to remove chemicals used for membrane preservation. Prior to each experiment, the membrane was stabilized (precompacted) at 20 bar using Milli-Q water until there was not observed further variation in permeate flux to avoid the influence of compaction during filtration experiments. The cross-flow velocity and feed pressure were controlled through adjustment of a bay-pass valve and a back pressure regulator. The operation time required for the membrane system to reach steady state was usually about 30–60 min. During the experiments, samples of permeate and concentrate solutions were collected every 20 min after the membrane system reached steady state. The volume of samples withdrawn for solute analysis was 5 ml.

3. Results and discussion

3.1. Evolution of the relative permeate flux

Fig. 2 compares the relative permeate flux of the NF-270 and NF-90 membranes during fouling development. Relative permeate flux, *RPF*, was calculated as the feed solution to pure water permeate flux ratio ($RPF = J_s/J_w$).

Relative permeate flux gradually decreased within the first 4 h of filtration. After 4 h of filtration, relative flux remained constant for NF-270, while a persistent slight diminution was found for the NF-90 membrane throughout the whole experiment. NF-90 membrane globally showed the widest flux decline during 7 h experiments (14% against 8%). RPF decrease may be caused by pore restriction and initial adsorption of the solutes on the membrane surface [18,19]. Solute adsorption is usually attributed to hydrophobic interaction with the active layer of the membrane. Since NF-90 hydrophobic character is higher than the corresponding to NF-270, as reflected by their respective contact angle (Table 2), the enhanced permeate flux diminution should be considered as the consequence of hydrophobic solutes adsorption on the NF-90 surface.

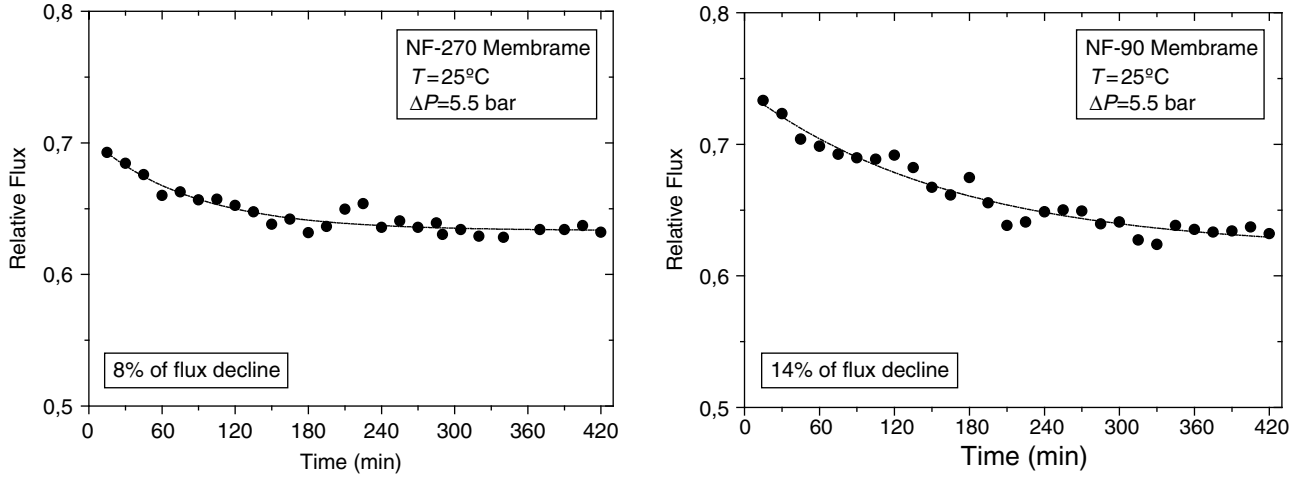

Fig. 2. Temporal evolution of the relative permeate flux for NF-270 and NF-90 membranes.

3.2. PhACs rejection

Rejection of pharmaceuticals as a function of time during filtration experiments with NF-270 and NF-90 membranes are displayed in Fig. 3. NF-90 rejection values measured for every selected solute are systematically higher than the corresponding to NF-270 as expected due to its smaller pore size and lower MWCO [13]. The observed rejection for the NF-90 membrane was quite similar for all the studied pharmaceuticals (over 95%). Conversely, NF-270 performance showed distinctive rejection for each compound with experimental values ranging from 75% (NCT) to 95% (RNT). Therefore, the further analysis was only focused on the NF-270 rejection performance.

The highest rejection differences, which were observed for RNT and NCT, could be explained in terms of steric hindrance considerations by assuming that molecular weight is an adequate parameter to reflect the molecular size. However, other interactions aside from size exclusion should be considered in order to explain why DCF and HCT with the same molecular weight are differently rejected by the NF-270 membrane. Electrostatic interactions between charged solutes and nanofiltration membranes, strongly related to solution pH, have been reported to be a significant rejection mechanism [20]. At experimental pH, around 7, acid constants (Table 2) evidence that HCT is mostly uncharged while anionic species are predominant for DFC. In addition, NF-270, as most polyamide membranes, is negatively charged at neutral pH due to deprotonation of carboxylic groups on the membrane surface [2]. So, the electrical repulsion between membrane surface and charged DFC species is assumed to remarkably increase the membrane rejection. It should be emphasized that the three solutes exhibiting rejection time evolution with apparent initial decline are compounds in neutral (HCT) or cationic form (RNT and NCT) at experimental pH. Although hydrophobic interactions can usually play

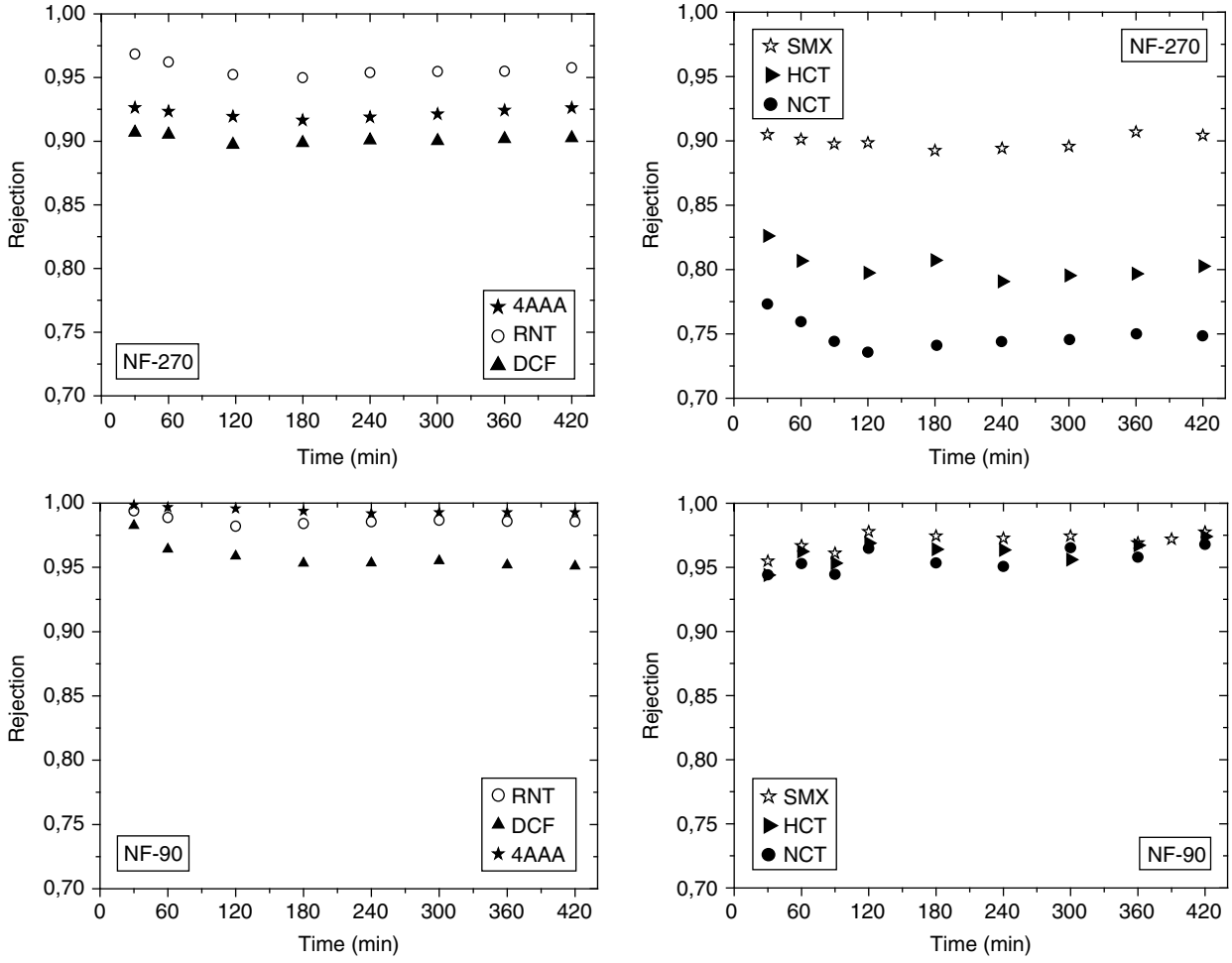

Fig. 3. Pharmaceuticals rejection by NF-270 and NF-90 membranes as a function of time. Experiments were conducted at 25 C and 5.5 bar.

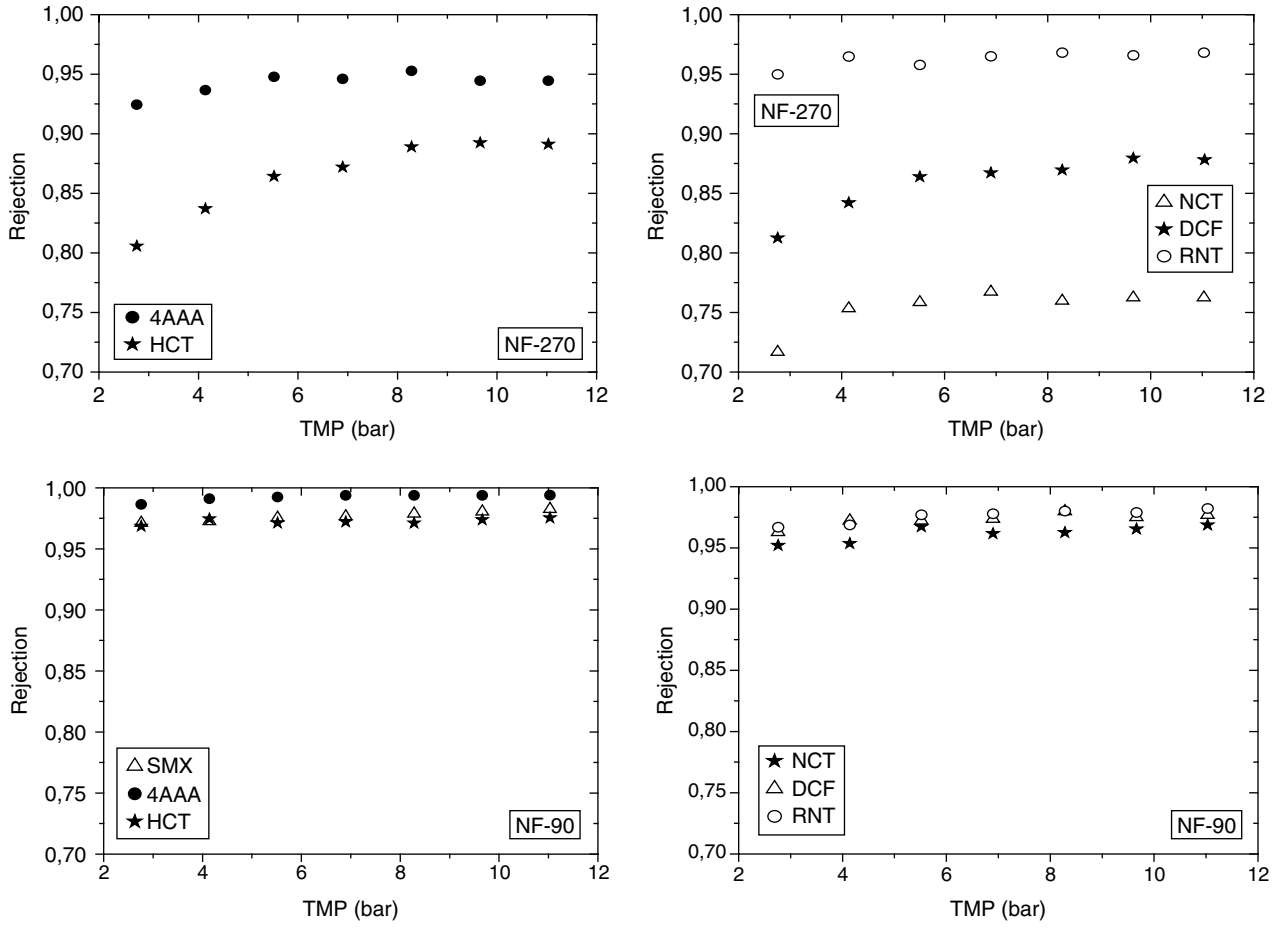

Fig. 4. Influence of transmembrane pressure on pharmaceuticals rejection at 25°C.

an important role on the membrane rejection of organic compounds minor effects are expected here because of the rather hydrophilic character of NF-270 membrane (low contact angle).

3.3. Influence of pressure on membrane rejection

It is well-known that the applied transmembrane pressure affect the separation performance, regardless to the separation mechanism. To investigate the pressure influence on pharmaceuticals rejection by NF-90 and NF-270, a collection of experiments were carried out at seven different transmembrane pressures in the 2–12 bar interval. The obtained results were plotted in Fig. 4. It is observed that the influence of pressure on NF-270 membrane performance is much more pronounced than for NF-90 membrane where rather flat rejection values are found. Conversely, the rejection of all pharmaceuticals by NF-270 exhibits an apparent increasing trend. At low pressure values, rejection of compounds varied almost linearly with applied pressure and then the rejection performance of membrane held constant.

4. Conclusions

The capability of nanofiltration for the separation of aqueous pharmaceuticals was investigated with two commercial membranes (NF-270 and NF-90). NF-90 membrane showed the highest flux decline during 7 h experiments (14% against 8%). Permeate flux decrease can be attributed to solute adsorption due to hydrophobic interaction with the membrane surface. All pharmaceutical rejections were very high for NF-90 (over 95%) and high for NF-270 (over 75%). So, it could be concluded that nanofiltration is suitable to remove pharmaceuticals from waste streams. The sequential rejection was analysed solely for NF-270. Steric hindrance and electric interaction in the solute/membrane interface were considered the main parameters determining the pharmaceuticals rejection. The importance of the solution chemistry (pH, speciation) on the membrane performance was discussed in terms of the charge repulsion between the negative charged membrane surface and anionic solute species. At last, rejection of pharmaceuticals by NF-270 membrane systematically raised when transmembrane pressure was increased.

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