Removal efficiency of pharmaceuticals in drinking water production

Application of nanofiltration

BTO 2012.008(s)
March 2012

KWR Watercycle Research Institute

BTO

KWR Watercycle Research Institute

Removal efficiency of pharmaceuticals in drinking water production

Application of nanofiltration

BTO 2012.008(s)
March 2012

Postbus 1072 3430 BB Nieuwegein The Netherlands P +31 30 606 95 11 F +31 30 606 11 65E info@kwrwater.nl

Colophon

Title
Removal efficiency of pharmaceuticals in drinking water production.
Application of nanofiltration

Project number
B111718-001

Research programme
Water Treatment

Project manager
Dirk Vries

Client
Board of Commissioners BTO

Quality Assurance
Erwin Beerendonk, Jan Post

Author(s)
Sabrina Botton and Emile Cornelissen

Sent to
PBC Waterbehandeling, Expert group Pharmaceuticals

Preface

Within the framework of the BTO program the project 'dealing with pharmaceuticals in drinking water production' investigates risk assessment and risk management options for pharmaceuticals and their metabolites in drinking water production. This project is a thematic integrated project within the KWR research groups 'Water Treatment' (WT) and 'Chemical Water Quality' (CW). The objective of this project is to determine the most efficient and sustainable approach to deal with pharmaceuticals in drinking water production. Various existing drinking water treatment methodologies (active carbon filtration, UV-H_2O_2 oxidation and membrane filtration) are assessed in terms of removal efficiency for pharmaceuticals and their metabolites. This report focuses on the application of nanofiltration for the removal of pharmaceuticals in drinking water production.

This report presents the outcome of a nanofiltration pilot test carried out at KWR. Nanofiltration represents an attractive treatment option for the removal of salts, particles, pathogens but also organic micro-pollutants. However, in order to fully exploit its potential, the underlying mechanisms of rejection need to be understood, especially under realistic operating conditions, namely in the presence of fouling constituents in the feed water. The research conducted at KWR aims at providing insight into the process of membrane filtration and its rejection behavior for a wide range of micro-pollutants by combining pilot testing with comprehensive membrane characterization.

The authors would like to acknowledge the contributions of Arne Verliefde (Ghent University and Delft University of Technology) and Tan Quach (Delft University of Technology) to this work. Also, the research could not have been successfully carried out without the practical help and continuous availability of Harry van Wegen and Sydney Meijering (Technical Workshop KWR). In addition, we would like to thank Anke Brouwer (Laboratory of Microbiology, KWR) for her assistance during membrane autopsies.

Sabrina Botton
Emile Cornelissen

Summary

The need for additional barriers for the removal of pharmaceuticals has gained increasing interest in the drinking water sector. High pressure membrane filtration might represent a cost-effective solution to the presence of this class of organic micro-pollutants in drinking water sources as high rejection efficiencies of micro-pollutants have been proved in recent research [1-6]

The mechanisms regulating the rejection of a broad range of physico-chemically diverse pharmaceuticals with a low molecular weight (< 300 g/mol) was investigated in a nanofiltration pilot installation and the removal efficiencies of a virgin and a fouled membrane were compared. In particular we have focused the present research on the effect of one specific fouling mechanism, namely biofouling, defined as the attachment and growth of bacteria leading to operational problems. Biofouling virtually affects any nanofiltration or reverse osmosis membrane installation hence its occurrence strongly affects the performance and efficiency of this filtration process. Biofouling has shown to cause several operational problems, like an increase in hydraulic resistance to permeate flow, leading to flux decline; higher frictional resistance over the membrane that increases the transmembrane pressure drop (related to the energy demand of the installation); hindered back diffusion of salts, resulting in elevated osmotic pressures at the membrane surface [7-9]. All these mechanisms have a direct and tangible effect on the performance of full scale-membrane plants and ultimately lead to increased maintenance costs, for example due to need of cleaning procedures to reduce flux decline. However, if the effects of hydraulic parameters are generally well understood, the influence of biofouling on rejection performance is yet unclear. Biofouling was shown to determine salt rejection decrease [9], but the effects of biomass growth and attachment on the membrane surface on the rejection of organic micro-pollutants still need to be assessed. A lower rejection of pharmaceutically active compounds upon biofouling could mean that membranes need to undergo more frequent or different clean in place procedures. Alternatively, it might be that biofouling offers a second barrier against the passage of pharmaceutical, thus resulting in increase rejection efficiency. Hence the removal of a wide range of pharmaceuticals varying in size, hydrophobicity and charge by a pilot-scale NF membrane installation was investigated in the presence and absence of biofouling and the results were compared and discussed.

Data presented in this work indicate that an average removal of 93% of the initial organic micro-pollutant concentration can be obtained on bench-scale (at a recovery of 10%) with a clean (virgin) nanofiltration membrane. Higher rejection values were generally observed for negatively charged pharmaceuticals compared to neutral and positively charged solutes. This behavior can be ascribed to the negative charge of the membrane surface that results in charge repulsion for negatively charged pharmaceuticals and in charge attraction for the positively charged solutes. A second membrane element was subjected to biofouling by dosing a readily biodegradable carbon source (Na-acetate) in the feed water. The development of biofouling was monitored by following the feed channel pressure drop increase in time [10]. Upon biofouling, corresponding to 150% pressure drop increase, a highly hydrated biofilm developed onto the biofouled membrane. The biomass layer had a negative impact on the rejection of most hydrophobic solutes (decrease in rejection), but a beneficial effect for small hydrophilic solutes (such as glycerol) (increase in rejection). The removal of pharmaceuticals on bench-scale (at a recovery of 10%) by a membrane subjected to biofouling was in average equal to 90%. Extrapolation of the measured rejection results to full-scale (at a typical recovery of 80%) will result in lower rejection values. For pharmaceuticals with a rejection of 85% at 10% recovery, the rejection decreases to 70% at 80%. For most part of the investigated pharmaceuticals full-scale nanofiltration will be an effective barrier against pharmaceuticals, even after extensive biofouling. Exceptions are some smaller hydrophobic pharmaceuticals which can potentially pass the membrane with more than 20%.

In summary, in both clean and biofouled membrane, positively charged pharmaceuticals present the lowest rejection compared to neutral and negatively charged solutes. Biofouling had a significant negative impact on positively charged of pharmaceuticals rejection, but left the retention of neutral and negatively charged of pharmaceuticals unaltered. The removal of positively charged solutes should therefore be carefully monitored in drinking water installation, especially at the onset of biofouling.

Membrane surface characterization and knowledge of the physico-chemical properties of the pharmaceuticals allowed distinguishing the different mechanisms governing solutes rejection. With the membrane employed in this research and the set of pharmaceuticals investigated, charge interactions predominated: electrostatic attraction between positively charged pharmaceuticals and negatively charged membrane surface and repulsion between the negatively charged pharmaceuticals negatively charged membrane surface played a major role. Secondly, hydrophobic interactions between hydrophobic membrane surface and hydrophobic pharmaceuticals resulted in a facilitated passage through the membrane for hydrophobic solutes.

The removal efficiency of small positively charged and hydrophobic pharmaceuticals should therefore be carefully monitored in full-scale installations as this class of organic micro-pollutants presents the lowest rejection in NF membrane and appears to be the most susceptible to a further rejection decrease as a consequence of biofouling development.

Contents

1 Introduction

Pharmaceuticals in drinking water production
Within the framework of the BTO program the project 'dealing with pharmaceuticals in drinking water production' investigates risk assessment and risk management options for pharmaceuticals and their metabolites in drinking water production. This project is a thematic integrated project within the KWR research groups 'Water Treatment' (WT) and 'Chemical Water Quality' (CW). The objective of this project is to determine the most efficient and sustainable approach to deal with pharmaceuticals in drinking water production. Various existing drinking water treatment methodologies (active carbon filtration, UV-H_2O_2 oxidation and membrane filtration) are assessed in terms of removal efficiency for pharmaceuticals and their metabolites. This report focuses on the application of nanofiltration for the removal of pharmaceuticals in drinking water production. The application of high pressure membrane filtration (i.e., nanofiltration (NF) and reverse osmosis (RO)) is rapidly evolving in drinking water production, owing to the cost competitive robust and reliable production of high quality water, with almost complete rejection of pathogens, salts, organic matter and organic micro-pollutants [1, 3, 4, 11].

Pharmaceuticals and interaction mechanisms
Pharmaceutically active compounds (PhACs) and their metabolites have been detected in aquatic environments at concentrations up to µg/l [12, 13]. As PhACs are designed to exert biological effects at low concentrations, their presence in drinking water sources is of great concern for drinking water companies and consumers. In fact, the need for additional barriers aimed at removing pharmaceuticals and hormonal disruptors has a high priority in the drinking water sector. Membrane filtration might represent a cost-effective solution to tackle the occurrence of PhACs in drinking water sources as high removal efficiencies of micro-pollutants have already been found [1, 2, 11]. The removal of lower molecular weight (MW) pharmaceuticals in NF installations might, in some cases, not be complete, even when the MW is larger than the molecular weight cut off (MWCO) of the membranes [11]. Usually the MWCO of the membrane is used to indicate the lower limit of molecules that cannot pass the membrane. However, other rejection mechanisms like hydrophobicity and charge interactions also play an important role in governing removal efficiencies [11, 14]. As the physico-chemical interplay between the membrane and the micro-pollutants regulates membrane rejection, the characterization of these interactions becomes fundamental to develop the most suitable barrier against PhACs in drinking water.

Operation and removal efficiency
Another important aspect to be considered is that, while operating a membrane installation, fouling problems might arise that could partially deteriorate the quality of the produced water. Due to the deposition of particles, salts, colloids and/or bacteria in time, the membrane surface will also be altered. This modification of membrane surface properties might lead to changes in solutes removal, as the above mentioned rejection mechanisms (steric exclusion, charge interactions and solute-membrane affinity) are largely governed by membrane surface properties [8, 11].

In order to assess the efficiency of membrane filtration in the removal of PhACs the following aspects were tackled with the present research:

- removal efficiency of a mixture of low molecular weight pharmaceuticals varying in size, charge and hydrophobicity;
- understanding the underlying rejection mechanisms by performing membrane surface characterization;
- investigating whether occurrence of biofouling could result in modified rejection efficiencies.

2 Material and Methods

2.1 Equipment and filtration protocol

A pilot plant consisting of two parallel membrane pressure vessels, each accommodating a single 2521 nanofiltration spiral wound membrane element was employed to perform membrane filtration experiments, see Figure 1 .

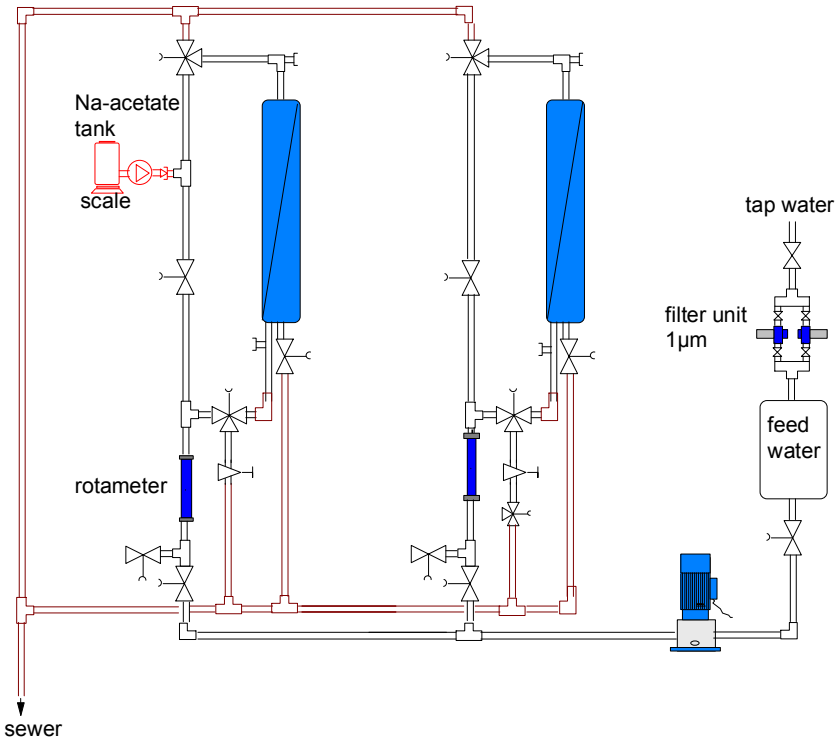

Figure 1 Schematic diagram of the pilot installation employed for filtration experiments..

Pre-filtered tap water (1 µm cartridge filters) from Nieuwegein, the Netherlands, was used as feed water, which was collected into a 1000 L buffer tank before being delivered to the membrane elements by a centrifugal pump. The experiments were carried out at a constant cross-flow velocity of 0.1 m/s and a feed flow of 350 L/h per pressure vessel, corresponding to practical conditions of full-scale membrane elements. Concentrate needle valves were used to set and maintain 10% recovery (corresponding to 35 L/h of permeate) during the test. Feed and permeate flows were monitored by Rota meters and feed water temperature was kept constant at 17±2°C.

One of the two elements was subjected to biofouling by dosing of an easily degradable carbon source (Na-acetate). The filtration protocol applied is schematically depicted in Figure 2. Biomass growth was stimulated by supplementing the feed water of one module with Na-acetate (1 µCarbon/L) with a dosing pump at a flow of 10 ml/min and the corresponding feed channel pressure drop increase (PDi) was monitored in time by a differential pressure drop meter. Once PDi reached 150%, Na-acetate dosing was stopped. In full scale NF plants, cleaning of the fouled elements is recommended by membrane manufacturers when normalized PDi reaches 10-15% over the entire installation [15]. However this measurement gives incomplete information about the condition of the PDi over the single elements

constituting the NF plant. In fact, a PDi of 10% for an installation consisting of a two staged (2:1) eighteen 4' elements might be the result of a PDi of 90% only for the first elements [15]. For this reason Na-acetate was dosed until PDi in the biofouled element reached 150%.

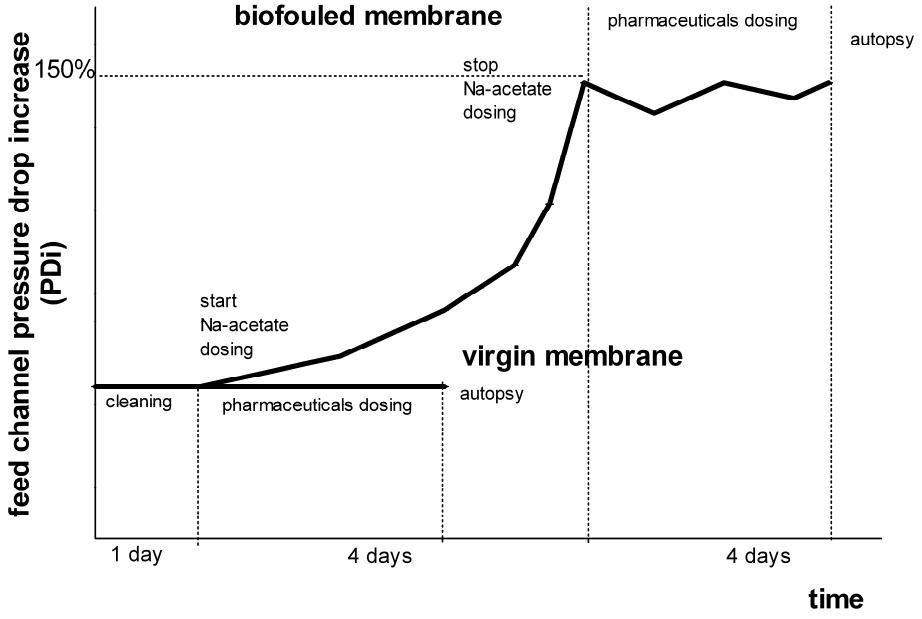

Figure 2. Schematic illustration of the filtration protocol applied for virgin and biofouled membranes.

In order to quantify rejection efficiency by the two membranes, a mixture of 23 pharmaceuticals (2 µg/L each in water, Table 1) was spiked from a 500 L stainless steel tank by a second centrifugal pump. Pharmaceuticals were dosed in recirculation mode with both concentrate and permeate recycled back into the feed tank. In order to avoid overestimation of rejection values due to incomplete adsorption of the solutes onto and within the membrane [16], the pharmaceuticals solution was circulated for 4 consecutive days. During the recirculation experiments the temperature was kept constant at 20 °C by a cooling device present in the feed tank.

2.2 Membrane characterization

The membranes used in this study were commercially available Desal HL 2521 thin film composite modules with a cross linked aromatic polyamide top layer. According to the membrane manufacturer, the membranes have a molecular weight cut off (MWCO) of 150-300 g/mol. The membranes were rinsed with tap water for several hours to remove preservatives the day before start-up.
At the end of the experiment, the membranes were carefully removed from the pressure vessel and drained to remove the excess of water. An autopsy was subsequently performed: virgin and biofouled membranes were cut open, unrolled and coupons were selectively cut out.

The zeta potential of samples (2x2 cm^2) originating from the middle part of the membrane were determined in duplicate in a 1mM KCl background solution (SurPASS, Anton Paar, Graz, Austria).

Three samples of approximately 10 cm^2 were cut out from the inside leaf of the module at the inlet, middle and outlet side for adenosine triphosphate (ATP) determination, a measure of biomass activity on the membrane surface. The ATP content of the obtained bacterial suspension was then quantified according to Magic-Knezev and Van der Kooij [17], the detection limit of this method is 0.004 ng ATP/cm^2.

The surface tension of membranes were determined by measuring the contact angle formed between a drop of liquid and the membrane surface [18]. Contact angle (θ) measurements are commonly employed to determine the surface energy via the Young-Dupré equation that links contact angle of a drop of

liquid (L) deposited on a flat solid surface (M) with the surface tension of the liquid (γ_L) according to [19]:

$$(1+\cos\theta)\gamma_L = 2\sqrt{\gamma_M^{LW}\gamma_L^{LW}} + \sqrt{\gamma_M^{+}\gamma_L^{-}} + \sqrt{\gamma_M^{-}\gamma_L^{+}}$$ Equation 1

The hydrated contact angle measuring technique was applied [19-21] to determine the contact angle value of three probe liquids, MilliQ water, glycerol and diiodomethane. The contact angles between membrane and probe liquids were determined employing a goniometer (Krüss DSA10, Krüss GmbH, Germany) equipped with contact angle calculation software (Drop Shape Analysis, Krüss GmbH, Germany). At least 10 measurements were performed on different locations of virgin and biofouled membranes for the sessile drop technique on the dry membrane. The surface tension components of the virgin and biofouled membrane can be determined after solving the above equations by measuring the contact angles between the membrane and three probe liquids of known γ_L^{LW}, γ_L^- and γ_L^+, namely water, glycerol and diiodomethane.

The free energy of cohesion ΔG_{MLM}, or hydrophilicity/hydrophobicity, defined by Equation 2, represents the relative energetic favourability of water molecules maintaining contact with the solid material rather than with each other [19].

$$\Delta G_{MLM} = -2\left(\sqrt{\gamma_M^{LW}} - \sqrt{\gamma_L^{LW}}\right)^2 - 4\left(\sqrt{\gamma_M^{+}\gamma_M^{-}} + \sqrt{\gamma_L^{-}\gamma_L^{+}} - \sqrt{\gamma_M^{-}\gamma_L^{+}} - \sqrt{\gamma_L^{-}\gamma_M^{+}}\right)$$ Equation 2

Positive values for this cohesion energy indicate that a positive amount of energy is required to expel water from the surface, in other words that the surface is hydrophilic. Negative values for the cohesion energy, on the other hand, suggest that it is energetically favourable for water to be expelled from the surface, and thus the surface can be defined as hydrophobic [19].

2.3 Pharmaceuticals and analysis

2.3.1 Pharmaceuticals

The pharmaceuticals investigated in this study, summarized in Table 1, were mainly selected based on their range of physico-chemical properties, to assess the relative influence of these parameters on solute rejection [22]. The selection procedure is entirely described in BTO-report 2011-100(s): "Selecting relevant pharmaceuticals and metabolites for monitoring, risk assessment and removal efficiency studies, version 1". Following physico-chemical properties were considered: (i) solute size: Solutes with molecular weight close to the MWCO of the membranes were selected. As model solutes for rejection experiments glycerol (propane-1,2,3-triol with a molecular weight of 92 g/mol) was used, (ii) hydrophobicity: expressed as logD (distribution coefficient) defined as the ratio of the equilibrium concentration of the sum of unionized and ionized species at pH 7.4 in two immiscible solvents, and (iii) charge at neutral pH.

Table 1. Physico-chemical characterization of the selected pharmaceuticals.

Pharmaceuticals	Function	MW (g/mol)	log K_{ow}	log D (pH7.4)	pK_a	Charge (pH 7)
Terbutaline	bronchodilator	225	0.9	-1.4	8.9	+
Salbutamol	bronchodilator	239	0.6	-1.9	9.3	+
Pindolol	beta blocker	248	1.8	0.1	9.2	+
Propranolol	beta blocker	259	3.5	1.3	9.6	+
Atenolol	beta blocker	266	0.2	-1.7	9.4	+
Metoprolol	beta blocker	267	1.9	-0.1	9.5	+
Sotalol	beta blocker	272	0.2	-1.6	9.4	+
Clenbuterol	bronchodilator	277	2.0	1.0	9.3	+
Trimethoprim	antibiotic	290	0.91	0.6	7.1	+/0
Phenazon	analgesic	188	0.4	0.3	1.4	0
Aminopyrine	analgesic	231	1.0	0.8	5	0
Carbamazepine	antiepilectic	236	2.5	1.9	n.a.	0

Cyclophosphamide	chemotherapy	260	0.6	0.2	0 ; 12.8	0
Pentoxyfilline	lipid regulator	278	0.3	0.3	0.3	0
Ibuprofen	analgesic	206	4.0	0.8	4.4	–
Clofibric acid	anti-cholesterol	214	2.6	-0.9	3.4	–
Naproxen	analgesic	230	3.2	0.5	4.2	–
Fenoprofen	anti-inflammatory	242	3.9	0.8	4.2	–
Gemfibrozil	lipid regulator	250	4.8	1.8	4.5	–
Sulfamethoxazol	antibiotic	253	0.9	-0.2	6.1	–
Ketoprofen	anti-inflammatory	254	3.1	-0.3	4.3	–
Diclofenac	analgesic	295	4.5	1.0	4.2	–
Bezafibrate	lipid regulator	362	4.3	0.7	3.4	–

2.3.2 Analysis

High performance liquid chromatography (HPLC) followed by tandem mass spectrometric detection was used to quantify the concentration of pharmaceuticals according to the method published by Sacher et al. [23]. Sample preparation and detailed description of the analytical methods can be found in the same work [23]. The detection limit was 10ng/L for the whole group of solutes, which were spiked as a mixture from a concentrated stock solution in water. The mixture of micro-pollutants was added, resulting in a concentration of 2µg/L for each compound. This concentration was selected to be able to accurately detect 99% rejection, corresponding to a permeate concentration of 20 ng/l.
Rejection (R) of the pharmaceuticals was calculated as follows:

$$R_i = 1 - (C_P/C_F) \qquad \text{Equation 3}$$

where C_P,i and C_F,i are the concentration of the pharmaceutical of interest (i) in the permeate and in the feed, respectively. Water samples were taken from the feed and permeate side of the NF membrane after four days continuous operation in recirculation mode. The concentration of the pharmaceuticals was determined from these water samples.

3 Results and Discussion

3.1 Membrane characterization

Surface properties of virgin and biofouled membranes were determined and compared in order to evaluate whether the presence of biofilm alters the surface characteristics, namely pore size, surface charge, surface energy and hydrophobicity which are the governing parameters in solutes rejection.

Table 2. Surface properties of clean and biofouled NF membranes

	predicted membrane pore size (nm)	surface charge (mV)	surface energy (mJ/m²)				ΔG_{MLM} hydrophilicity (mJ/m²)	ATP (ng/cm²)
				apolar	polar			
			γ^{TOT}	γ_{LW}	γ^+	γ^-		
virgin	0.6	-33±7	**56.7**	23.9	5.4	49.2	21.3	
biofouled	0.5	-35±7	**54.3**	19.5	5.3	57.6	27.9	2.9

To determine the pore size (r_p) of the membranes, a transport model earlier developed by Verliefde et al [24] was fitted to the experimentally obtained rejection values of a model organic solute (glycerol) by the virgin and biofouled membranes [20, 24]. By using an optimization procedure (Solver, Excel) the best fit for the pore size was then found equal to 0.6 and 0.5 nm for clean and biofouled membranes, respectively, Table 2. The biofilm consists of bacteria and a variety of organic molecules [25]. Some of these biopolymers could accumulate onto and penetrate into the membrane thus partially narrowing its average pore size (and porosity).

Streaming current measurements showed how the surface charge of virgin and biofouled membrane remains practically unaltered, being equal to -33 and -35 mV, respectively at pH 6-8 (Table 2). It can be concluded that biomass attachment did not significantly modify surface charge and pore size. Values measured for the virgin membrane are in agreement with previously published data [13, 26].

Contact angle measurements were carried out to determine surface tension of virgin and biofouled membranes while they are fully hydrated [20]. In accordance with current knowledge, membranes present a predominant electron donor functionality (γ^-) and an increase in membrane surface hydrophilicity (ΔG_{MLM}) occurs upon biomass attachment, in agreement with the presence of a highly hydrated biofilm [20].

Biomass accumulation on the membrane surface was monitored by ATP measurements, which revealed that 2.5, 1.0 and 3.4 ± 0.1 ng ATP/cm2 accumulated at the feed side, in the middle and at the brine side of the module, respectively. According to previous research, development of biofouling (PDi 10-100%) onto NF membranes by Na-acetate dosing induces an accumulation of biomass that corresponds to 1-5 ng/cm2 ATP [27], in agreement with the values presented here.

3.2 Pharmaceutical rejection

3.2.1 Charge interactions

Rejection values measured for each investigated pharmaceutical are above 85% for the virgin membrane, as can be seen in Figure 3A, in agreement with previous studies [13, 22, 26]. In general it can be observed that positively charged pharmaceuticals display only slightly lower rejections than the negatively charged and neutral organic solutes, likely as consequence of electrostatic repulsion with the membrane

surface [3, 13, 22, 28]. Due to the negative charge of the membrane surface, positively charged pharmaceuticals are attracted towards the membrane and this electrostatic attraction results in the lower observed rejection values. For the negatively charged solutes, the opposite holds, whereas for neutral solutes no charge interactions occur.

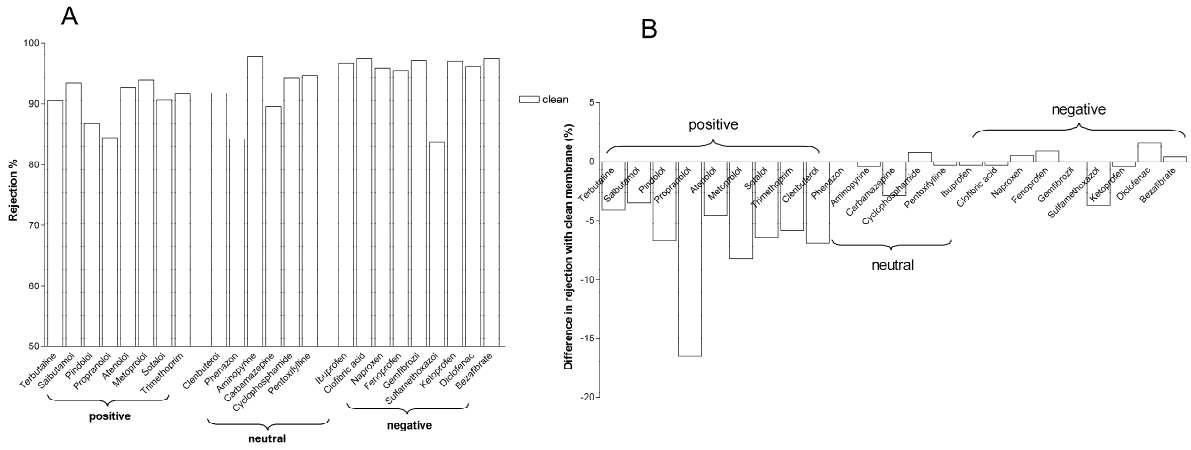

Figure 3. (A) Rejection by a clean membrane and (B) absolute difference in rejection between virgin and biofouled membranes

When the rejection values of the solutes by the clean membrane are compared to the values measured with the biofouled one, the difference in behavior among the differently charged groups becomes more evident, Figure 3B. In fact, positively charged PhACs were generally more affected by the presence of the biofilm layer, with significant decrease in their removal (up to 17% absolute decrease in rejection). Rejection of neutral and negatively charged solutes, on the other hand, did not change notably. Lower rejections for positively charged pharmaceuticals upon biofouling development are probably due to a combination of different phenomena. Occurrence of biofilm into which PhACs can accumulate probably results in an increased concentration of pharmaceuticals at the membrane surface: bacterial cells growing on the membrane and the dense layer in which they are embedded hinder the back-diffusion of solutes, which leads to increased concentration polarization phenomena. In the case of biofouling, this process is probably enhanced by the attractive forces occurring between negatively charged biomass and the positively charged pharmaceuticals.

3.2.2 Hydrophobic interactions

The surface energy of a selection of 14 pharmaceuticals employed in the spiking test were experimentally determined using pressed pharmaceuticals tablets, see Table 3, and the obtained total surface energy values are in good agreement with available chemical databases [20]. Surface tension components were subsequently applied to determine the free energy of interaction between solute and membranes, ΔG. ΔG can in simple terms be viewed as the amount of energy required or obtained from the interaction between the objects being considered, in this case pharmaceuticals and membrane surface immersed in water. Positive values of ΔG indicate that the interaction between a specific pharmaceutical and the membrane is not energetically favorable or that repulsion occurs. Negative ΔG, on the contrary, implies attraction.

All organic micro-pollutants exhibited a positive ΔG, for both virgin and biofouled membranes, indicating the occurrence of repulsive forces between pharmaceuticals and membranes. This suggests that no spontaneous transfer of solute molecules from the water phase to the membrane phase will occur.

The hydrophobic affinity between solute and membrane is clearly altered by the deposition of the biofilm onto the membrane surface, as indicated by the consistent increase in $\Delta G_{biofouled}$ compared to ΔG_{virgin} for twelve of the fourteen investigated solutes of Table 3.

Table 3. Surface tension (γ) components of a selection of pharmaceuticals and interaction energy of these solutes with virgin and biofouled membranes. All values are expressed as mJ/m². Table modified from [20].

Surface energy / PhACs	γ_{Tot}	ΔG_{virgin}	$\Delta G_{biofouled}$
Terbutaline	58.6	5.6	6.7
Propranolol	48.6	6.8	4.6
Atenolol	25.8	5.4	6.7
Metoprolol	44.7	10.5	6.7
Sotalol	42.9	7.8	9.2
Trimethoprim	43.5	7.5	9.1
Aminopyrine	48.3	7.8	9.2
Carbamazepine	46.5	5.4	6.6
Pentoxifylline	45.2	8.0	9.5
Ibuprofen	37.9	0.7	1.7
Clofibric acid	45.4	5.2	6.3
Naproxen	43.1	1.9	3.0
Gemfibrozil	39.1	1.0	2.1
Diclofenac	39.3	9.2	10.9

When the rejection is related to the free energies of interaction reported in Table 3, the contribution of solute-membrane affinity emerges, as demonstrated by the corresponding trends depicted in Figure 4.

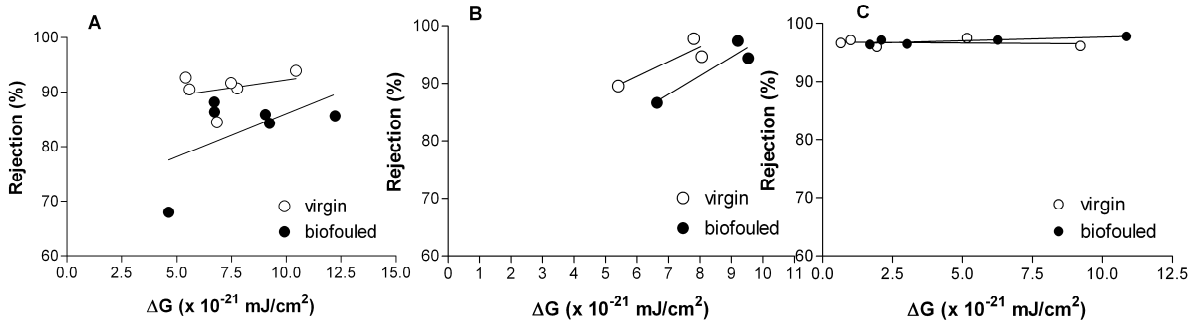

Figure 4.Rejection of (A) positively charged, (B) neutral and (C) negatively charged solute by biofouled membrane as a function of interaction energy between solutes and virgin (ΔGvirgin) and biofouled (ΔGbiofouled) membranes. Lines indicate the linear regression

Table 3 demonstrates that the modification of membrane surface properties as a result of biomass attachment and growth is consistently affecting the affinity between the different solutes and the membrane. Figure 4 suggests that when the interaction energy (ΔG) between a certain PhACs is higher, an increase in rejection can be expected. This behavior is easily explained: a higher ΔG means that the system solute-membrane requires more energy to interact or that repulsion between solute and membrane occurs. If solute and membrane repel each other, an increase in rejection can be expected. Lower ΔG, on the other hand, implies that attraction between solutes and membrane is taking place. Hydrophobic attraction will lead to a decrease in rejection. More data would be needed to confirm the

trends observed in Figure 4B. In general, Figure 4 indicates that higher values for ΔG lead towards a less spontaneous transfer of the solute through the membrane, thus resulting in a higher rejection. Higher affinity (decreasing values of ΔG), induces the opposite behavior.

For neutral solutes, no electrostatic interactions occur and the small differences in behavior of three of the neutral pharmaceuticals employed in the spiking test are solely controlled by solute-membrane affinity. As shown in Figure 4B, a significant correlation appears between rejection and ΔG_{virgin} and $\Delta G_{biofouled}$, indicating that the removal of the neutral pharmaceuticals used in this study, is predominantly controlled by solute-membrane hydrophobic affinity.

For negatively charged solutes, the absence of slope in rejection *versus* ΔG curves (as depicted in Figure 4C) suggests that the rejection of negatively charged solutes is largely independent from ΔG. This is mainly due to the prevailing effect of electrostatic repulsion between these negatively charged solutes and the negative membrane surface charge.

4 Discussion and conclusions

Nanofiltration can efficiently remove a broad range of diverse organic micro-pollutants. The removal was on average equal to 93% and 90% for clean and biofouled membrane respectively. Higher rejection values were generally observed for negatively charged pharmaceuticals compared to neutral and positively charged solutes. This behavior can be ascribed to the negative charge of the membrane surface that results in charge repulsion for negatively charged PhACs and in the accumulation of positively charged solutes on the membrane surface. Upon biofouling, a highly hydrated biofilm developed onto the biofouled membrane, conferring a higher hydrophilicity to the membrane. This modification had a negative impact on the rejection of more hydrophobic solutes, but a beneficial effect for small hydrophilic one (like glycerol) [20].

Nanofiltration experiments conducted in this research were operated at a system recovery of 10%. Full-scale membrane systems operating on ground or surface water operate at much higher recoveries ranging between 75%-85%. At higher recovery values the solute concentration is higher in the membrane elements, for example at a recovery of 80% the solute concentration is five times higher compared to the feed concentration at the inlet. Rejection values decrease when the solute concentration increases. The expected PhACs rejection values on full-scale NF are therefore lower than the determined PhACs values on bench-scale. For solutes with a rejection of 85% at 10% recovery, the rejection decreases to 70% at 80% [5]. For this study this means that for a virgin NF membrane, the rejection of propanolol, phenazon and sulfamethoxazol on full-scale NF is expected to be lower than 80%. For the other investigated compounds the rejection on full-scale is expected to be higher than 80%. In the case of severe biofouling especially the positively charged PhACs are affected, resulting in an expected drop in rejection of particularly pindalol and propanolol.

The knowledge gained in this research will be beneficial for full-scale drinking water production plants, as it confirms that NF represents an efficient filter for the majority of the pharmaceuticals investigated, irrespective of charge, hydrophobicity and size. In addition, it indicates that, even in case of severe biofouling, NF installations can still offer an efficient barrier to the passage of most of the investigated organic micro-pollutants. However, the data gained in the present research also indicates that special attention should be devoted to the monitoring of small positively charged and hydrophobic solutes. The rejection of these classes of solutes will decrease, due to the occurrence of concentration polarization processes and will be more affected by the occurrence of biofouling.

A high pressure membrane process, such as reverse osmosis (RO), can be applied to reject PhACs from drinking water sources. RO membranes are very dense and form a robust barrier for the rejection of emerging substances, such as PhACs, from groundwater or surface water. The major disadvantage of these membranes is the relatively high pressure which is required to facilitate sufficient water transport through the membrane. NF membranes are more open compared to RO membranes but require less energy. The balance between PhACs rejection and energy requirement will depend on the specific water quality of the source water. On the basis of this research, we concluded that NF is a robust barrier for most investigated PhACs. When a specific water source is impaired by pindalol, propanolol, phenazon and sulfamethoxazol NF alone might not be a sufficient barrier. An alternative for membrane filtration is using oxidation processes, which is the topic of parallel research track within the BTO pharmaceutical project. An possible disadvantage of using oxidation techniques is the formation of by-products from the reaction with natural organic matter from sources of drinking water. Energetically, using oxidative techniques is favorable compared to high pressure membrane processes.

NF can be a robust barrier for PhACs depending on the presence of the type of PhACs in sources for drinking water. Particularly smaller, positively charged and hydrophobic solutes such as pindalol (relatively hydrophobic, positively charged), proponolol (hydrophobic, positively charged) and phenazon (small) can pass a NF on full-scale to more than 20% (less than 80% rejection). Hydrophobic solutes can be effectively adsorbed by activated carbon filtration (ACF), therefore a NF followed by ACF seems to be a synergistic combination. NF followed by ACF offers multiple advantages, such as a robust

barrier for a broad range of PhACs and an elongated lifetime of ACF columns because of the removal of natural organic matter by preceding the NF process. This approach is currently under investigation in an international Innowator project ESTAB ('emerging substances towards an absolute barrier'). In this 3-year project KWR, Pentair X-flow, Delft University of Technology, Oasen, Vitens, Veolia Water Solutions, Epas, VMW (Vlaamse Maatschappij voor Watervoorziening), KompetenzZentrum Wasser (KZW) Berlin and Berliner Wasserbetriebe participates.

5 References

1. Kimura, K., et al., *Rejection of organic micro-pollutants (disinfection by-products, endocrine disrupting compounds, and pharmaceutically active compounds) by NF/RO membranes.* Journal of Membrane Science, 2003. **227**(1-2): p. 113-121.
2. Kimura, K., et al., *Rejection of neutral endocrine disrupting compounds (EDCs) and pharmaceutical active compounds (PhACs) by RO membranes.* Journal of Membrane Science, 2004. **245**(1-2): p. 71-78.
3. Nghiem, L.D., A.I. Schaefer, and M. Elimelech, *Pharmaceutical Retention Mechanisms by Nanofiltration Membranes.* Environmental Science & Technology, 2005. **39**(19): p. 7698-7705.
4. Nghiem, L.D., A.I. Schafer, and M. Elimelech, *Removal of Natural Hormones by Nanofiltration Membranes: Measurement, Modeling, and Mechanisms.* Environmental Science & Technology, 2004. **38**(6): p. 1888-1896.
5. Verliefde, A.R.D., et al., *Construction and validation of a full-scale model for rejection of organic micro-pollutants by NF membranes.* Journal of Membrane Science, 2009. **339**(1-2): p. 10-20.
6. Verliefde, A.R.D., et al., *Rejection of trace organic pollutants with high pressure membranes (NF/RO).* Environmental Progress, 2008. **27**(2): p. 180-188.
7. Flemming, H.C., *Biofouling in water systems – cases, causes and countermeasures* Appllied Microbiology and Biotechnology, 2002. **59**(6): p. 629-40.
8. Flemming, H.C., et al., *Biofouling--the Achilles heel of membrane processes.* Desalination, 1997. **113**(2-3): p. 215-225.
9. Herzberg, M. and M. Elimelech, *Biofouling of reverse osmosis membranes: Role of biofilm-enhanced osmotic pressure.* Journal of Membrane Science, 2007. **295**(1-2): p. 11-20.
10. Vrouwenvelder, J.S., et al., *Pressure drop increase by biofilm accumulation in spiral wound RO and NF membrane systems: role of substrate concentration, flow velocity, substrate load and flow direction.* Biofouling, 2009. **25**(6): p. 543-555.
11. Bellona, C., et al., *Factors affecting the rejection of organic solutes during NF/RO treatment-a literature review.* Water Research, 2004. **38**(12): p. 2795-2809.
12. ter Laak, T.L., et al., *Relating environmental concentrations of pharmaceuticals to consumption: A mass balance approach for the river Rhine.* Environment International, 2010. **36**(5): p. 403-409.
13. Verliefde, A.R.D., et al., *Influence of electrostatic interactions on the rejection with NF and assessment of the removal efficiency during NF/GAC treatment of pharmaceutically active compounds in surface water.* Water Research, 2007. **41**(15): p. 3227-3240.
14. Verliefde, A.R.D., *Rejection of organic micro-pollutants by high pressure membranes (NF/RO)*. 2008, TU Delft: Delft.
15. van Der Kooij, D., W.A.M. Hijnen, and E.R. Cornelissen, *Biofouling of Spiral-Wound Membranes in Water Treatment*. 2010, Denver, CO: Water Research Foundation.
16. Kimura, K., et al., *Adsorption of hydrophobic compounds onto NF/RO membranes: an artifact leading to overestimation of rejection.* Journal of Membrane Science, 2003. **221**(1-2): p. 89-101.
17. Magic-Knezev, A. and D. van der Kooij, *Optimisation and significance of ATP analysis for measuring active biomass in granular activated carbon filters used in water treatment.* Water Research, 2004. **38**(18): p. 3971-3979.
18. van Oss, C.J., *Development and applications of the interfacial tension between water and organic or biological surfaces.* Colloids and Surfaces B: Biointerfaces, 2007. **54**(1): p. 2-9.
19. van Oss, C.J., *Interfacial forces in aqueous media*. 2006, Boca Raton, FL: Taylor & Francis Group.
20. Botton, S., et al., *Influence of biofouling on pharmaceutical rejection in high pressure filtration.* Submitted for publication, 2011.
21. Bouchard, C.R., et al., *Study of humic acid adsorption on nanofiltration membranes by contact angle measurements.* The Canadian Journal of Chemical Engineering, 1997. **75**(2): p. 339-345.
22. Verliefde, A.R.D., et al., *The role of electrostatic interactions on the rejection of organic solutes in aqueous solutions with nanofiltration.* Journal of Membrane Science, 2008. **322**(1): p. 52-66.
23. Sacher, F., et al., *Pharmaceuticals in ground waters: Analytical methods and results of a monitoring program in Baden-WÃ¼rttemberg, Germany.* Journal of Chromatography A, 2001. **938**(1-2): p. 199-210.

24. Verliefde, A.R.D., et al., *Influence of Solute-Membrane Affinity on Rejection of Uncharged Organic Solutes by Nanofiltration Membranes.* Environmental Science & Technology, 2009. **43**(7): p. 2400-2406.
25. Liu, H. and H.H.P. Fang, *Extraction of extracellular polymeric substances (EPS) of sludges.* Journal of Biotechnology, 2002. **95**(3): p. 249-256.
26. Verliefde, A.R.D., et al., *Influence of membrane fouling by (pretreated) surface water on rejection of pharmaceutically active compounds (PhACs) by nanofiltration membranes.* Journal of Membrane Science, 2009. **330**(1-2): p. 90-103.
27. Hijnen, W.A.M., E.R. Cornelissen, and D. van der Kooij, *Threshold concentrations of biomass and iron for pressure drop increase in spiral-wound membrane elements.* Water Research, 2010. **45**(4): p. 1607-1616.
28. Xu, P., et al., *Effect of membrane fouling on transport of organic contaminants in NF/RO membrane applications.* Journal of Membrane Science, 2006. **279**(1-2): p. 165-175.

Postbus 1072 3430 BB Nieuwegein The Netherlands P +31 30 606 95 11 F +31 30 606 11 65 E info@kwrwater.nl