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Edyta KUDLEK[1*], Jolanta BOHDZIEWICZ[1]
and Mariusz DUDZIAK[1]

# INFLUENCE OF WATER MATRIX ON THE RETENTION OF PHARMACEUTICALS BY HIGH-PRESSURE MEMBRANE FILTRATION

## WPŁYW MATRYCY WODNEJ NA RETENCJĘ FARMACEUTYKÓW W WYSOKOCIŚNIENIOWEJ FILTRACJI MEMBRANOWEJ

**Abstract:** High-pressure membrane processes, including nanofiltration and reverse osmosis, allow for the removal of a wide range of organic micropollutants (including pharmaceutical compounds) from water streams. Those processes also may be an effective method for in-depth treatment of water containing pharmaceutical compounds. The paper presents a comparison of retention of selected pharmaceuticals from the group of non-steroidal and anti-inflammatory drugs, *ie* ibuprofen and diclofenac and psychotropic drugs – carbamazepine, present in various aqueous matrices in the nanofiltration process. Deionized water based solutions as well as model and real wastewater effluents after biological treatment processes were subjected to the filtration process. The nanofiltration process was carried out in a cross-flow tubular membrane filtration system. Three polyamide membranes AFC30, AFC40 and AFC80 from PCI Membrane System Inc were used. It has been found, that the retention of pharmaceutical compounds increased with the membrane filtration time, regardless of the composition of the treated aqueous matrix. Moreover, the presence of inorganic compounds and high-molecular organic substances had a positive effect on the membrane separation process of micropollutants.

**Keywords:** diclofenac, ibuprofen, carbamazepine, nanofiltration

## Introduction

The escalating problem of the presence of a wide range of pharmacological substances in the environment becomes one of topical research issues, which are currently being undertaken in the field of environment engineering and protection. Excessive consumption of medicines belonging to the group of biologically active substances may compromise the stability of many ecosystems, especially of water

[1] Institute of Water and Wastewater Engineering, Silesian University of Technology, ul. Konarskiego 18, 44–100 Gliwice, Poland, phone: +48 32 237 16 98, fax: +48 32 237 10 47.

* Corresponding author: edyta.kudlek@polsl.pl

ecosystems [1]. The Directive of the European Parliament and of the Council 2013/39/EU of 12 August 2013 [2] ordered the monitoring of substances listed in the decision of the Executive Commission (EU) 2015/495 of 20 March 2015 [3]. Apart from nine other organic micropollutants includes diclofenac. That substance watch list includes, among others, pharmaceutical compounds from the group of non-steroidal and anti-inflammatory drugs – diclofenac and synthetic hormones – 17-alpha-ethinyl-estradiol. The data obtained during the monitoring will allow to determine whether these pharmaceutical compounds should be classified as one of the priority substances, and thereby force the need to develop methods for their effective elimination from the aquatic environment.

Among the unconventional methods, which allow for the treatment of water streams from a wide range of organic micropollutants, high-pressure membrane processes *ie* nanofiltration and reverse osmosis are mentioned. The effectiveness of those processes depends on many factors which include operating parameters of the process, the physicochemical properties of used membranes and removed compounds as well as on the chemical composition of the treated water matrix [4, 5].

The aim of the study was to determine the influence of the chemical composition of water matrices on the retention degree of pharmaceutical compounds from the group of non-steroidal and anti-inflammatory drugs – diclofenac and ibuprofen and psychotropic drugs – carbamazepine in the nanofiltration process. The high-pressure membrane filtration process was carried out in the cross-flow mode using a semi-industrial installation equipped with a tubular membrane module. Three types of polyamide membranes AFC30, AFC40 and AFC80 from PCI Membrane System Inc. (USA) were tested. In addition, a description of the separation mechanisms, which determine the retention of micropollutants was undertaken.

## Materials and methods

The study on the effectiveness of the removal of pharmaceutical micropollutants in the nanofiltration process was carried out using three water matrices *ie* a solution prepared based on deionized water and a real and model effluent from a mechanical--biological wastewater treatment line (Table 1). To all water matrices selected patterns of micropollutants were added.

Table 1

Physicochemical characteristics of examined water solutions

| Water matrix | Deionized water | Model effluent* | Real effluent |
|---|---|---|---|
| pH | 7.00 | 7.10 | 7.15 |
| Conductivity [mS/cm] | 0.271 | 0.992 | 1.109 |
| Absorbance ($\lambda$ = 254 nm) [$nm^{-1}$] | 0.038 | 0.064 | 0.269 |
| TOC [$mg/dm^3$] | 5.02 | 29.25 | 30.16 |

* The model effluent was prepared on the basis of tap water and dry nutrient broth, casein peptone, $NH_4Cl$, NaCl, $CaCl_2 \cdot 6H_2O$, $MgSO_4 \cdot 7H_2O$, $K_2HPO_4$ and $KH_2PO_4$.

The concentration of tested pharmaceutical compounds in water solutions was established at 1 mg/dm$^3$. Analytical standards of non-steroidal and anti-inflammatory drugs in the form of diclofenac (DCL) and ibuprofen (IBU) sodium salts and the psychotropic drug – carbamazepine (CBZ) were purchased from Sigma-Aldrich (Poznan, Poland) (Table 2).

Table 2

Characteristics of pharmaceutical micropollutants

| Pharmaceutical compound | Diclofenac sodium salt | Ibuprofen sodium salt | Carbamazepine |
|---|---|---|---|
| Symbol | DCL | IBU | CBZ |
| Molecular formula | $C_{14}H_{10}Cl_2NNaO_2$ | $C_{13}H_{17}O_2Na$ | $C_{16}H_{12}N_2O$ |
| Molecular weight [g/mol] | 318.13 | 228.26 | 236.3 |
| Solubility in $H_2O$ [mg/dm$^3$] | 50 | 100 | 17 |
| $pK_a$ | 4.15 | 4.91 | 2.30 |
| log $K_{ow}$ | 4.51 | 3.97 | 2.45 |
| Stokesa radius [nm] | 0.414 | 0.295 | 0.319 |

The nanofiltration process was operated in a cross-?ow mode using a semi-industrial installation TMI 14 from J.A.M INOX Produkt equipped with a tubular flow-through membrane module with a polyamide membrane from PCI Membrane System Inc. (USA) (Table 3). The membrane total surface area was 240 cm$^2$. The filtration process was conducted for 180 min to collect 20 % of the initial volume of the feed.

Table 3

Characteristics of used membranes

| Membrane type | AFC30 | AFC40 | AFC80 |
|---|---|---|---|
| Skin layer-material | polyamide | polyamide | polyamide |
| Molecular weight cut-off [Da] | 200 | 200 | < 200 |
| NaCl retention [%] | 75 | 60 | 80 |
| $MgSO_4$ retention [%] | 90 | 92 | 98 |
| pH range | 1.5–9.5 | 1.5–9.5 | 1.5–10.5 |
| Hydrophilicity* | 4 | 4 | 4 |

* 1 – low hydrophilicity, 5 – high hydrophilicity.

In the initial step of the study the impact of the transmembrane pressure on the transport properties of used membranes was assessed (Fig. 1). The volumetric permeate flux of deionized water free of pharmaceutical compounds was determined according to

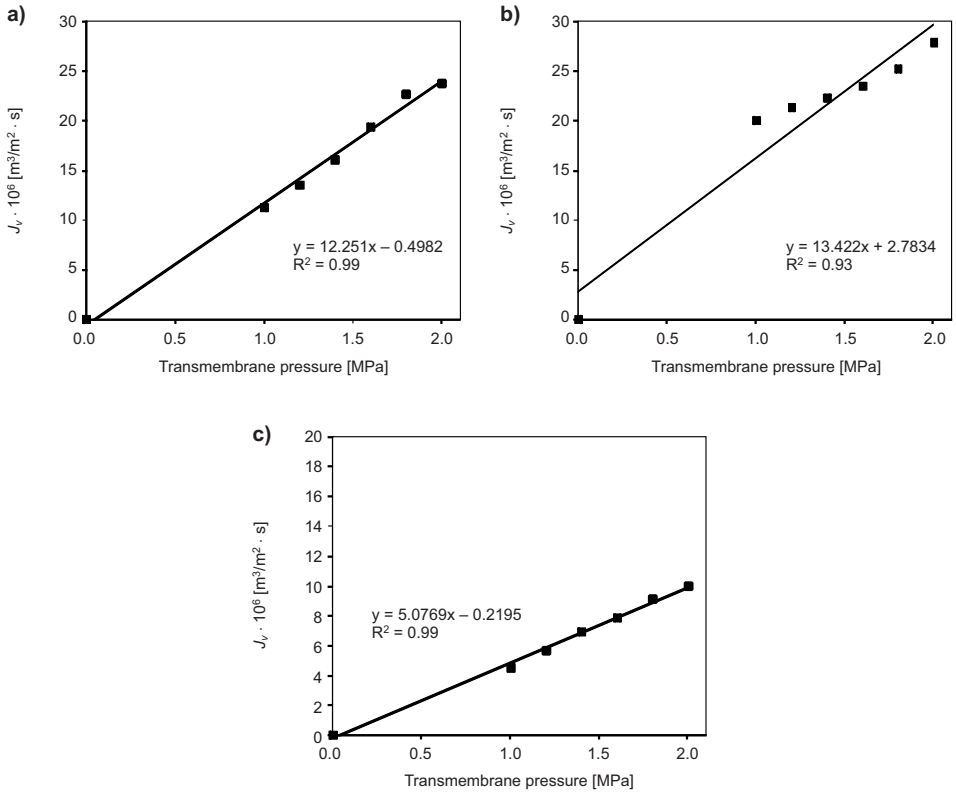


Fig. 1. Influence of transmembrane pressure on the value of the permeate volumetric flux (membrane a) AFC30, b) AFC40 and c) AFC80)

equation (1). The process transmembrane pressure used in the study was assumed at the level of 2 MPa.

$$J_v = \frac{V}{F \cdot t} \tag{1}$$

where: $J_v$ – volumetric permeate flux [$m^3/m^2 \cdot s$];
$V$ – permeate volume [$m^3$];
$F$ – membrane surface area [$m^2$];
$t$ – filtration time [s].

The retention degree of pharmaceutical micropollutants, which was determined on the basis of equation (2), estimate the effectiveness of the process.

$$R = \left(1 - \frac{C_f}{C_0}\right) \cdot 100\,\% \tag{2}$$

where: $R$ – retention degree [%];
$C_p$ – pharmaceutical concentration in the permeate [mg/dm$^3$];
$C_f$ – pharmaceutical concentration in the feed [mg/dm$^3$].

The concentration of the tested pharmaceuticals was examined by the use of HPLC chromatography combined with UV detection preceded by solid phase extraction SPE (sample preparation stage for chromatographic determination). During the SPE extraction disposable Supelclean ™ ENVI-8 columns (volume 6 cm$^3$ and 1.0 g phase) from Supelco (Poznan, Poland) were applied. In order to solvation the octylsilane ($C_8$) column bed was washed with 5 cm$^3$ of methanol and then conditioned with the same volume of deionized water at pH 7. Next water sample of a volume of 20 cm$^3$ was added to the extraction cartridge. After the extraction the column bed was dried under vacuum. The obtained extract was eluted with 3 cm$^3$ of methanol and subjected to drying in a stream of technical nitrogen. Prior to the chromatographic determination the eluent was dissolved in 0,1 cm$^3$ of methanol. For the analysis a Varian (Warszawa, Poland) high performance liquid chromatograph equipped with a Hypersil GOLD column from Thermo Scientific (Warszawa, Poland) with a length of 25 cm, a diameter of 4.6 mm and a pore size of 5 μm were used. A mixture of acetonitrile/water in the proportions of 85:15 (v/v) was applied as the mobile phase.

## Results and discussion

Figure 2 shows the retention coefficient for the tested pharmaceutical micropollutants obtained during the filtration of the solution prepared on the basis of deionized water. With the increasing filtration time, the reduction in the concentration of micropollutants was observed. This tendency was particularly observed in the case of IBU by the use of AFC80 membrane. The retention coefficient of that pharmaceutical compound was about 27 % after 15 minutes of filtration and after 120 minutes, reached the value of 54 %, while after 180 minutes exceed 88 %. The observed tendency is not typical compared to the results presented in papers in this field, where the retention of micropollutants usually decreases with the time of membrane filtration [6]. In the case of examined pharmaceuticalsthis relationship might have been caused by the change of the charge of the membrane surface due to the deposition in the skin layer and in the pores of negatively charged DCL molecules ($pK_a$ = 4.15), or neutral CBZ molecules ($pK_a$ = 2.30).

Among factors affecting the retention of organic micropollutants the physicochemical properties of the removed of compounds should been mentioned next to the load of the membrane surface. This is connected with the coexistence of three different mechanisms, which are responsible for the separation of compounds in the nanofiltration process [7] *ie* the exclusion mechanism, resulting from the so-called spheric effect, the electrostatic repulsion and physicochemical interaction occurring at the same time between the micropollutants, compounds of the treated solution and the surface of the membrane. In the initial stage of filtration for the AFC40 and AFC80 membranes (respectively to 105 and 45 min), it was observed that the retention of pharmaceuticals depended on their molar mass, which refers to the spherical construction of each

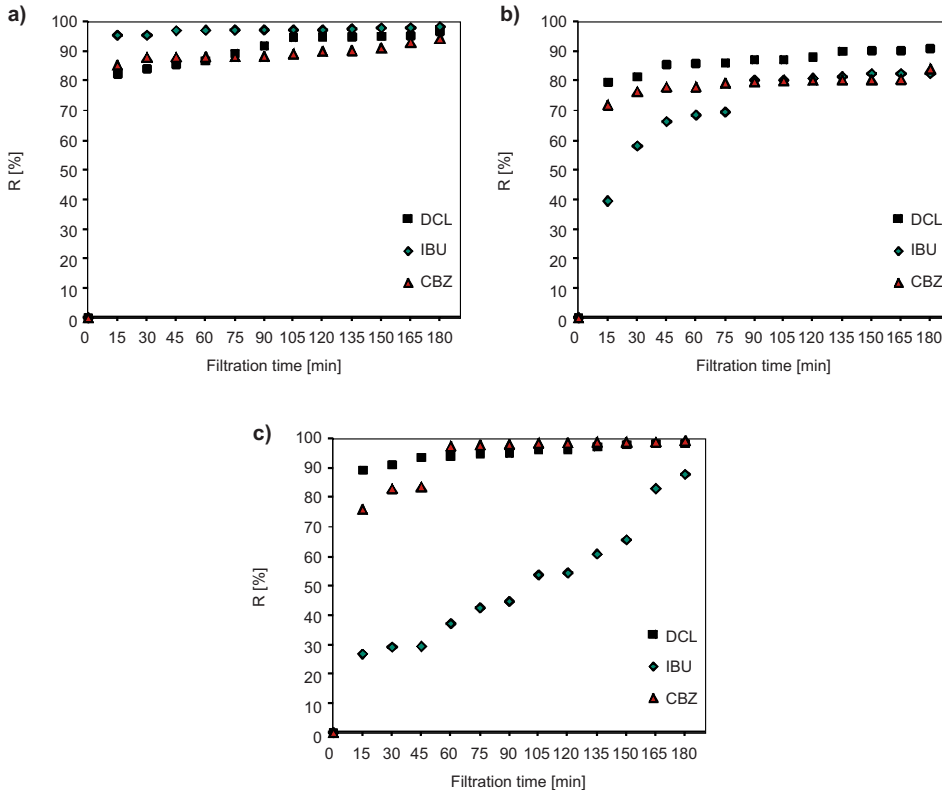


Fig. 2. Effect of the filtration time on the retention coefficient of deionised water spiked with pharmaceutical compounds (membrane a) AFC30, b) AFC40 and c) AFC80)

compound [8]. This dependence has also been confirmed by other researchers [9]. The highest removal degree in the process carried out by the use of the AFC80 membrane was observed for DCL (the retention coefficient after 45 minutes of filtration amounted to over 93 %) with a molecular weight equal to 318.13 g/mol and the lowest removal degree for IBU, which have a molecular weight of 228.26 g/mol (retention coefficient does not exceed 30 %). This demonstrates that the dominant mechanism of separation was the molecular sieving mechanism. On the other hand, during the continuation of the filtration so significant difference in the retention of examined pharmaceuticals were no longer observed. The determined retention values of DCL and CBZ were similar. This might be caused by the fact that both compounds are also characterized by a lower water solubility than the IBU. By contrast, the results presented in [10] indicated, that a low solubility of a compound in water indicates its high ability to be separate by the use of high pressure membrane processes. Therefore it can be assumed that at the subsequent stage of filtration the separation efficiency depended mainly on the exclusion mechanism (Table 2) and electrostatic repulsion, which is associated with the change of the membrane charge.

The molecular sieving mechanism also decided on the effectiveness of the process carried out using a AFC40 membrane. The highest removal degree was achieved for DCL (the retention coefficient after 180 minutes of filtration exceed 91 %), and the lowest for IBU, which amounted to around 82 %. For the AFC30 membranes it was observed, that the retention coefficient of micropollutants increases with the increasing pKa value of removed pharmaceuticals. The removal degree of negatively charged molecules of IBU ($pK_a$ = 4.91) exceeded 98 %, while the CBZ molecules, which belonging to substance endowed with a neutral charge, were retained only in 94 %. It can be assumed, that the separation of pharmaceutical compounds by the use of a AFC30 membrane, which have a negative charge during the implemented process conditions (pH = 7), resulted from the Donnan exclusion mechanism.

In the next stage of the study the filtration of model (Fig. 3) and real effluent (Fig. 4) spiked with pharmaceutical patterns was undertaken. In the first 45 minutes of filtration the values of the retention coefficient of all three examined pharmaceutical compounds, which were present in both matrices, increased in comparison to those observed in the case of filtration of the deionized water matrix. For example, the retention degree of pharmaceutical agents after 45 minutes of filtration of the real effluent by the use of

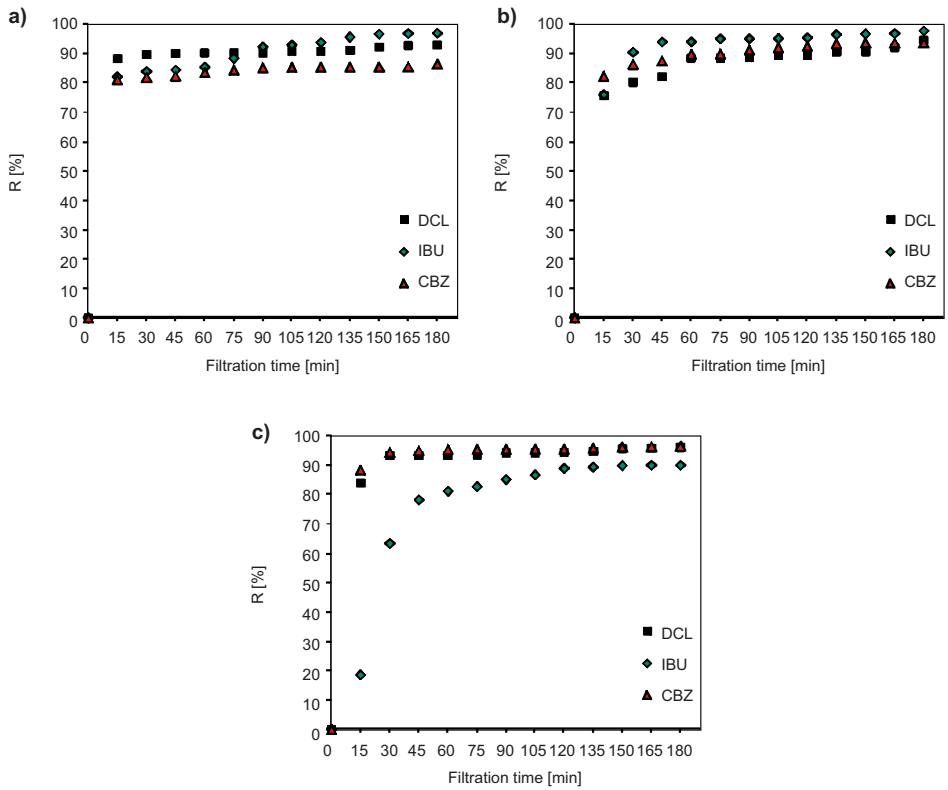


Fig. 3. The retention coefficient of drugs during the nanofiltration process of model wastewater effluent (membrane a) AFC30, b) AFC40 and c) AFC80)

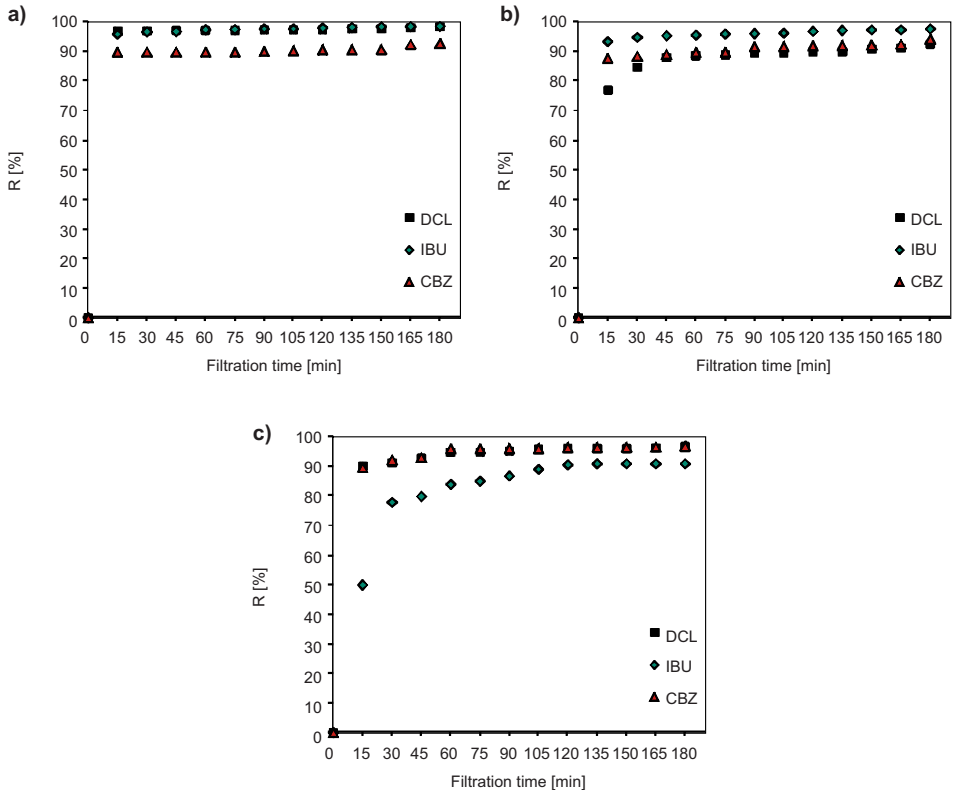


Fig. 4. The retention coefficient of pharmaceutical micropollutants during the nanofiltration process of real wastewater effluent (membrane a) AFC30, b) AFC40 and c) AFC80)

AFC80 membrane amounted respectively about 93 % for DCL and CBZ, and 80 % for IBU molecules. The retention of pharmaceutical compounds occurring in the real effluent after 15 minutes of filtration through the AFC30 membrane exceed 90 % and maintained at this level during 180 minutes of the process duration.

However the retention degree of DCL and CBZ designated for the AFC80 membrane between 60 and 180 minutes of filtration of both effluents received a relatively stable value, which exceeded 94 % for DCL and 95 % for CBZ. It should be emphasized that the retention of pharmaceuticals for the deionized water solution ranged from 75 % to 99 % depending on the type of the compound and filtration time. The reason for this phenomena may be the presence of inorganic compounds in the treated solution, particularly $Ca^{2+}$ ions, which are able to reduce the charge of the membrane surface resulting in the reduction of the retention of negatively charged molecules of micropollutants [12]. It can be assumed that during the filtration of solution containing organic and inorganic substances (model and real effluent) the separation mechanism of pharmaceutical compounds was completely different than in the case of filtration of solution prepared based on deionized water.

The highest retention degree of DCL and IBU present in real effluent was reported for the AFC30 membrane and exceeded 98 %, whereas CBZ was most efficiently retained on the AFC80 membrane. The membrane, which allowed for the most effective separation of micropollutants from the deionized water solution was the AFC80 membrane. An exception was only the IBU retention coefficient, which was at the highest level for the AFC30 membrane, and adopts a value of about 98 %. The increasing retention of pharmaceutical compounds occurring in water matrices with different chemical composition relative to matrices prepared on deionized water can be attributed, especially in the initial filtration time to the ability of micropollutants to bind to functional groups of high-molecular-organic compounds and form of so-called macromolecular complexes, which are featured with a higher retention than single micropollutants [11]. The presence of high-molecular-weight organic compounds in solutions results in the formation of an additional filtration barrier in the form of a so-called secondary membrane on the membrane surface. This phenomenon leads to the increase of filtration resistance and consequently increases the retention degree of low-molecular-weight pharmaceutical compounds. The formation of a secondary membrane as a result of the fouling phenomenon was confirmed by the determination of the permeate volumetric flux, which in case of the filtration of model and real effluent decreased by more than 7 % regarding to the filtration efficiency obtained for deionized water (Fig. 5). Indirectly, it was also evidenced by the fact that the increase in IBU retention was much faster during filtration of model or real effluent (Fig. 3 and 4) than during the filtration of the solution based on deionized water (Fig. 2).

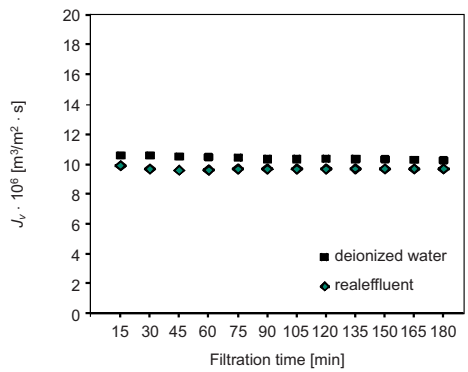


Fig. 5. Influence of water matrix on the value of the volumetric permeate flux (membrane AFC80)

## Conclusions

The efficiency of the filtration process depended strictly on physicochemical properties of removed organic micropollutants, as well as on the membrane surface charge and the composition of the feed. In addition, type of the dominant separation mechanism was changing with the filtration time and the occurrence of the fouling phenomena, which typically occured during the membrane filtration.

With the filtration time, the reduction in the concentration of pharmaceutical micropollutants was observed. The retention degree of DCL and CBZ after 15 min of filtration of all tested matrices exceeded 76 %. In the case of IBU that value amounted about 50 % for the AFC80 membrane and increased with the filtration time and the increasing of the fouling phenomena.

The separation process of DCL and CBZ was most efficient in the case of filtration of deionized-water based solutions by the use of AFC80 membrane. However, the degree of IBU retention achieved the highest value during the filtration of the model effluent using AFC40 membrane. It can be assumed, that the presence of high--molecular organic substances resulted in the formation of so-called "secondary membrane" on the membrane surface, which contributes to improvement of the separation properties of low-molecular-weight organic micropollutants.

## References

[1] Aga DS. Fate of Pharmaceuticals in the Environment and in Water Treatment Systems. Boca Raton: CRC Press. Taylor Francis Group; 2008.
[2] Directive 2013/39/EU of the European Parliament and of the Council of 12 August 2013 amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. Official J Europ Union. 2013;L 226;1-17. http://faolex.fao.org/docs/pdf/eur127344.pdf
[3] Commission Implementing Decision (EU) 2015/495 of 20 march 2015 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council. Official J Europ Union. 2015;78;40-42. http://faolex.fao.org/docs/pdf/eur142647.pdf
[4] Feng L, van Hullebusch ED, Rodrigo MA, Esposito G, Oturan MA. Chem Eng J. 2013;228;944-964. DOI: 10.1016/j.cej.2013.05.061
[5] Sin J-C, Lam S-M, Mohamed AR, Lee K-T, Int J Photoenergy. 2012;2012;1-23. DOI: 10.1155/2012/185159
[6] Xu P, Drewes JE, Kim T-U, Bellona C, Amy G. J Membr Sci. 2006;279;156-175. DOI: 10.1016/j.memsci.2005.12.001
[7] Radjenović J, Petrović M, Ventura F, Barceló D. Water Res. 2008;42;3601-3610. DOI:10.1016/j.watres.2008.05.020.
[8] Vergili I. J Environ Manage. 2013;127;177-187 DOI:10.1016/j.jenvman.2013.04.036
[9] Verliefde ARD, Cornelissen ER, Heijmana SGJ, Petrinic I, Luxbacher T , Amy GL, et al. J Membr Sci. 2009; 330; 90-103. DOI:10.1016/j.memsci.2008.12.039
[10] Dolar D, Košutić K. Compre Anal Chem. 2013;62;319–344. DOI:10.1016/B978-0-444-62657-8.00010-0
[11] Dolar D, Vuković A, Asperger D, Kosutić K. J Environ Sci (China). 2011;23;1299-1307. DOI: 10.1016/S1001-0742(10)60545-1
[12] Bellona C, Drewes JE. J Membr Sci. 2005;249;227-234. DOI:10.1016/j.memsci.2004.09.041

## WPŁYW MATRYCY WODNEJ NA RETENCJĘ WYBRANYCH FARMACEUTYKÓW W WYSOKOCIŚNIENIOWEJ FILTRACJI MEMBRANOWEJ

Wydział Inżynierii Środowiska i Energetyki
Politechnika Śląska

**Abstrakt:** Wysokociśnieniowe procesy membranowe, do których zaliczamy nanofiltrację i odwróconą osmozę, pozwalają na oczyszczenie strumieni wodnych z szerokiej gamy mikrozanieczyszczeń organicznych. Mogą znaleźć również zastosowanie w doczyszczaniu wód pod kątem eliminacji związków farmaceutycznych. W pracy przedstawiono porównanie stopnia retencji wybranych farmaceutyków z grupy niesteroido-

wych leków przeciwbólowych i przeciwzapalnych, tj. ibuprofen i diklofenak oraz leków psychotropowych – karbamazepina, obecnych w różnych matrycach wodnych w procesie nanofiltracji. Oczyszczaniu poddano roztwory sporządzone na bazie wody zdejonizowanej oraz modelowy i rzeczywisty odpływ po biologicznym oczyszczaniu ścieków. Proces nanofiltracji prowadzono w układzie filtracji krzyżowej przy zastosowaniu rurowego modułu membranowego. Oceniono efektywność procesu przy wykorzystaniu trzech poliamidowych membrana, tj. AFC30, AFC40 i AFC80 firmy PCI Membrane System Inc. Określono, że wraz z czasem filtracji membranowej wzrasta stopień retencji badanych związków farmaceutycznych niezależnie od składu oczyszczanej matrycy wodnej. Ponadto stwierdzono, że obecność w roztworze związków nieorganicznych oraz wysokocząsteczkowych substancji organicznych wpływa korzystnie na proces membranowej separacji mikrozanieczyszczeń.

**Słowa kluczowe:** diklofenak, ibuprofen, karbamazepina, nanofiltracja