Chemical cleaning of adsorbed pharmaceutical on NF/RO membranes

Dolar D.[1,*], Radoš J.[1], Ašperger D.[1], Košutić K.[1]

[1]Faculty of Chemical Engineering and Technology, University of Zagreb, Marulićev trg 19, Zagreb, HR-10000 Croatia

*corresponding author:

e-mail: dolar@fkit.hr

Abstract Nanofiltration (NF) and reverse osmosis (RO) have proved to be effective in the removal of various pharmaceuticals. One of the main rejection mechanisms is interaction/adsorption since pharmaceuticals, especially hydrophobic, adsorb on membrane polymeric matrix. Albendazole as hydrophobic pharmaceutical passed through 6 different NF/RO membranes (NF, NF90, NF270, BW30, UTC-70HA and XLE) at a pressure of 10 bar. Adsorption was confirmed with increase in concentrations of albendazole in permeate, and therefore decrease in rejection factor, and appearance of new peaks (showing new bonds) on Fourier transformation infrared (FTIR) spectra. Commercially available cleaning solution (Nalco PC99) was used to remove adsorbed albendazole from the membranes. FTIR spectra were used to confirm efficacy of cleaning agent. The results showed that commercially available cleaning solution was not appropriate for removal of adsorbed hydrophobic compound. FTIR spectra after adsorption and after chemical cleaning were similar showing that bonds (direct H-bonding between H of the OH group and N of the heterocyclic ring, stretching of C=C double bond in aromatic ring, string bending of the methyl group) between membrane polymeric matrix and albendazole were still present.

Keywords: adsorption, pharmaceutical, cleaning, nanofiltration, reverse osmosis

1. Introduction

Pharmaceutically active compounds (PhACs) can be found worldwide in various environmental matrices in ng/L to mg/L range [1-3]. Pressure membrane processes of nanofiltration (NF) and reverse osmosis (RO) have proved to be effective in the removal of various pharmaceuticals [4] via three main rejection mechanism (size exclusion, electrostatic repulsion/attraction, and interactions/adsorption) [5].

Numerous studies showed that hydrophobic compounds adsorb both on the membrane surface and deeper into the membrane structure [6-11]. Mainly feed concentration [12, 13], retention [7, 12, 14], and flux [11, 15] decreases. At the same time permeate concentration increases as function of time [7, 9, 12].

In the membrane processes, membrane cleaning is one of the most important concerns. A large number of chemical cleaning agents are commercially available. Alkali, acids, metal chelating agents, surfactants, and enzymes presents main categories of cleaning agents and a mixture of these chemicals, with unknown composition, represent commercial cleaning agents [16]. For example, acid cleaning is suitable for the removal of precipitated inorganics (scaling), while alkali cleaning is used to remove adsorbed organics [17].

In last ten years significant number of papers were publish in terms of impact of chemical cleaning (alkali and acidic) on NF and RO membranes properties (permeability, pore size, surface charge, surface morphology, and hydrophobicity) [16, 18-25] followed up with the effect of chemical cleaning on the removal of PhACs [19, 21-25].

Nevertheless, no information on chemical cleaning of adsorbed pharmaceuticals on NF/RO membranes has been reported. Therefore in this work, experimental study on NF and RO for removal of albendazole was carried out. There were two major goals. One was to determine adsorption of albendazole on commercial NF/RO membranes. The adsorption of albendazole was determined by measuring concentrations of albendazole in feed and permeate, calculating rejection and with Fourier transformation infrared (FTIR) spectra. The other was to use commercial chemical cleaning agent to clean fouled membranes, i.e. to desorb albendazole from polymeric matrix of the used NF/RO membranes.

2. Methods

2.1. NF/RO membranes

Six kinds of commercial membranes from Dow-Filmtec, USA (NF, NF90, NF270, BW30 and XLE) and Toray, Japan (UTC-70HA) were used. All membranes were stored at 7 ºC in the dark place until used. Molecular weight cut-off (MWCO) of the RO membranes was 100 Da, while in the case of nanofiltration was 150-300 Da. The operational pH range recommended by the manufacturer is between 2 and 11. However, for cleaning purposes, the pH can be lowered for a short-term cleaning (30 min) to pH 1 or increased to pH 12. The maximum operational temperature is 45 ºC taking into account that temperature should not exceed 35 ºC above pH 10.

2.2. Chemicals

Albendazole, as a hydrophobic pharmaceutical, was of the analytical grade (>99%) and obtained from Veterina (Kalinovica, Croatia). A stock solution of pharmaceutical (10 mg/L) was prepared in MilliQ water. Characteristics of albendazole are presented in Dolar *et al*. (2017) [26].

2.3. Infrared spectrometer with Fourier transformation

Membrane samples were characterized by means of FTIR spectroscopy using a Bruker Vertex 70 equipped with a Platinum ATR single reflection diamond (n=2.4) crystal-based module in the mid infrared (IR) range (400-4000 cm^{-1}). Infrared spectra of membranes were recorded at 4 cm^{-1} resolution and 32 scans were made before and after tests with pharmaceuticals.

2.4. Analytical methods

The liquid chromatographic analyses were performed using Varian ProStar 500 (Walnut Creek, California, USA), HPLC system consisting of a ProStar autosampler 410, ProStar 230 tertiary pump system, ProStar 330 diode array (DAD) detector, and a thermostated column compartment. HPLC separations were performed on InertSustain™ C18 column, (250 mm x 4.6 mm, 5 µm), GL Sciences Inc., Japan. The analysis was performed using 0.01% formic acid in MilliQ water as eluent A and 0.01% formic acid in acetonitrile as eluent B in gradient elution mode. After gradient elution, the column was equilibrated for 5 min before another injection. Flow rate was 0.5 mL/min. An injection volume of 30 µL was used in all analysis. The studied pharmaceutical was monitored at 210 nm (t_R=22.720 min) on a DAD. The column temperature was set to 30 ºC. Method detection limit (MDL) was determined by analysis of spiked MilliQ water samples, as the concentration that give S/N ratios of 3. The MDL value for albendazole was 0.006 mg/L.

2.5. Membrane cleaning reagent

The commercially available alkali cleaning reagent Nalco PermaClean99 (Nalco PC99, Nalco Europe, Leiden, Netherland) was selected in this study. Nalco PC99 was supplied in liquid form and a chemical cleaning solution (1.5% w/w) was prepared by diluting in demineralized water, resulting in a clear liquid with a pH of 12.23. According to manufacturer, PC99 contains a potassium hydroxide (5% w/w).

2.6. NF/RO system

This study was tested in a laboratory set-up (described in details by Dolar *et al*. (2011) [27] at a working pressure of 10 bar, flow rate 750 mL/min and the surface area of the membranes 11.0 cm^2.

İn order to dissolve the conserving agents, pristine membranes were washed with around 10 L of demineralized water without pressure, and then pressurized at 15 bar for 2 h. The experiment with albendazole was carried out in the batch circulation mode (permeate and concentrate streams circulated back to the feed tank) during 4 h to accomplish saturation of the membranes (steady state). Samples of feed were taken every hour, and permeate samples at the beginning and the end of the treatment. Membranes were cleaned with prepared chemical cleaning solution at 33.2±0.3 ºC. Firstly, cleaning solution recirculated 30 min at an elevated temperature followed by 30 min soaking of membranes. Subsequently the membranes were washed with copious amount of demineralized water. Clean (virgin) and chemically cleaned membranes were analyzed with FTIR.

3. Results and discussion

3.1. Adsorption of albendazole on NF/RO membranes

Adsorption of albendazole was monitored through rejection factor, concentration of albendazole (in feed and permeate streams), and FTIR spectra of the membranes. In Table 1 and 2 are presented rejection factors and concentrations of albendazole in permeate at the beginning and the end of the treatment, and concentrations of albendazole in feed stream during whole treatment, respectively. Albendazole is a hydrophobic compound tending to adsorb both on the membrane surface and deeper into the membrane structure [7-9]. Thus, rejection factors decreased during 4 h treatment for all investigated membranes [7, 13, 14] which is related to increase of albendazole concentrations in permeate [7, 9, 12] showing adsorption onto membrane polymeric matrix. Consequently albendazole diffused through the membranes resulting in feed concentration increase (Table 2).

Table 1. Rejection factors and concentrations of albendazole in permeate at the beginning and the end of the treatment

***t* / h**	**NF**	**NF90**	**NF270**	**BW30**	**XLE**	**UTC-70HA**
				R_f / %		
0	73.9	79.1	64.8	78.5	78.3	77.7
4	44.9	62.4	45.6	62.8	64.8	62.4
				γ(permeate) / mg/L		
0	4.06	3.24	5.36	3.33	3.32	3.39
4	5.56	3.79	5.66	3.75	3.66	3.91

Table 2. Concentrations of albendazole in feed stream during whole treatment

t / h	*γ* / mg/L
0	7.41
1	6.57
2	6.05
3	5.89
4	4.94

In Figure 1 are presented FTIR spectra for pristine membranes (black line), for membranes after treatment of albendazole (red line), and after cleaning with Nalco PC99 solution (blue line). The difference between pristine membranes and membranes after treatment of albendazole strongly indicate adsorption on membrane structure. New peaks (pointed up with arrows), i.e. bonds were present (in details in next paragraph).

3.2. Cleaning of adsorbed albendazole on NF/RO membranes

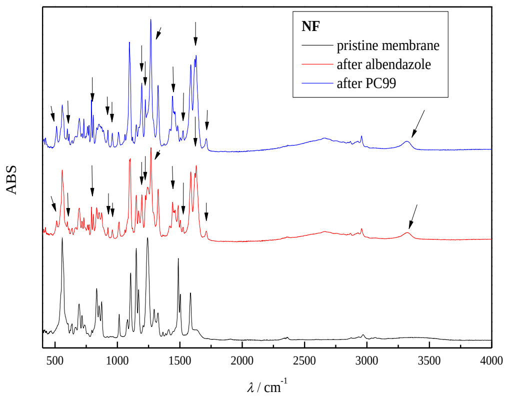
Before using a chemical cleaning solution for desorption of albendazole from the membranes, effect of this solution to the membrane structure was investigated (not presented here). FTIR spectra showed no discernible variations in peak after exposing the membranes to chemical cleaning solutions. Fujioka *et al.* (2014) [19] also showed no changes in FTIR spectra after exposing the membranes to chemical cleaning reagents. These results suggest that hydrolysis of the polyamide skin layer did not occur.

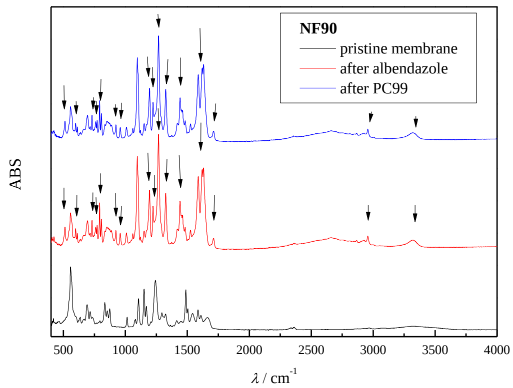
In Figure 1 FTIR spectra (red lines) presents interactions of albendazole and membrane structure. For all investigated membranes direct H-bonding between H of the OH group and the nitrogen of the heterocyclic ring (3320 cm^{-1}) was observed and was still present after cleaning. For BW30 and XLE membranes it can be observed that the whole baseline in the 2150-2820 cm^{-1} region moved up showing that cleaning was not efficient in cleaning of albendazole bonded on the membrane surface (this region shows binding of albendazole on the membrane surface due to its physicochemical characteristics). Dipole moment orientation of albendazole enables that 2-methylcarbamoyl substituent entered the membrane structure while ethyl group at the end of the molecule (aliphatic part) lags behind. At 771 and 792 cm^{-1} the bending of CH_2 in the aliphatic part of albendazole was detected before and after cleaning. Furthermore, according to Figure 1 new bond of the carbonyl group of albendazole (1620 and 1632 cm^{-1}), stretching of C=C double bond in an aromatic ring located in the polyamide top layer (1400-1525 cm^{-1}), $C(sp^2)–O–C(sp^3)$ bonds (1269 cm^{-1}), C–O–C bending bonds (1194 cm^{-1}), and string bending of the methyl ($–CH_3$) group of albendazole (800-1000 cm^{-1}) were detected.

The same results, new peaks, were obtained for investigated NF membranes due to similar structure of theirs.

As showed on Figure 1 (blue lines) it can be seen that all peaks formed on membranes after treatment of albendazole were not removed by chemical cleaning with Nalco PC99 agent. These results showed that albendazole was still bonded on polymeric matrix of all investigated membranes.

Since adsorption is one of the rejection mechanisms of pharmaceuticals (especially hydrophobic) with NF/RO membranes, the next goal of this research will be investigation of appropriate cleaning solution and cleaning conditions to remove adsorbed pharmaceuticals from membranes structure.





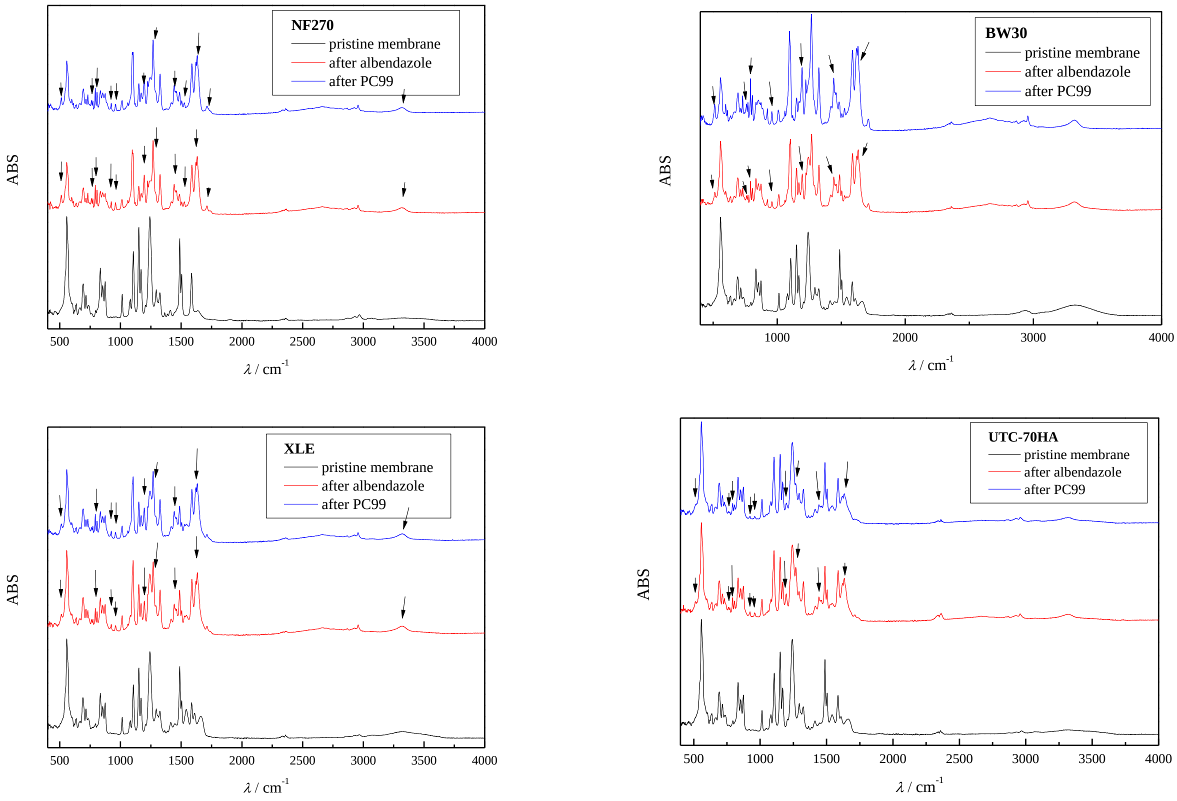


Figure 1. FTIR spectra of pristine membranes, membranes after treatment of albendazole, and after cleaning with Nalco PC99

Conclusions

Concentration of albendazole in feed (decrease) and permeate (increase) streams, rejection factors (decrease) and FTIR spectra (new peaks) confirmed adsorption of albendazole on RO (XLE, BW30, and UTC-70HA) and NF (NF, NF90, and NF270) membranes. FTIR spectra as a tool to confirm an efficacy of membrane cleaning showed that all created bonds and interactions between membranes and albendazole were still present after cleaning. Therefore, it can be concluded that commercial chemical cleaning agent and cleaning conditions were not appropriate to desorb albendazole from investigated NF/RO membranes.

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